2011

The Epidemiology of Human Rabies Postexposure Prophylaxis in Virginia, 2002 and 2003

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Master of Public Health Research Project

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by

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April 28, 2005

To Al, Eric, Juliet, and Genevieve for your patience and understanding

Acknowledgements

I would like to thank the following people and departments for their support and generous assistance in the development, conduct, and presentation of this study.

Virginia Department of Health
- Suzanne R. Jenkins, V.M.D., M.P.H, Diplomate ACVPM – Preceptor
- The many Virginia health district staff that assisted in the retrieval of data for this study
- Division of Zoonotic and Environmental Epidemiology
- Division of Surveillance and Investigation
- Jessie Hamlin
- Jerry O. Russell

Department of Epidemiology and Community Health – Virginia Commonwealth University
- Elizabeth Eustis Turf, PhD – Advisor
- Tilahun Adera, MPH, PhD
- C.M.G. Buttery, MD, MPH
- Saba W. Masho, MD, MPH
- Diane Bishop
- Karen P. Bryant
- Rhonda B. Stanfield
- Kate Young

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Abstract

Objective: To describe a sample that received human rabies postexposure prophylaxis (PEP) in Virginia as a result of animal exposures in 2002 and 2003 and to determine the extent to which PEP decisions were appropriate.

Methods: PEP surveillance data were requested from 35 Virginia health districts within 5 regions. Retrospective chart review was used to gather demographic, exposure and source animal data from patient records and animal exposure reports. Descriptive statistics are presented. True exposures and appropriateness of PEP were defined using the *2004 Virginia Rabies Control Guidelines* and the *Recommendations of the 1999 Advisory Committee on Immunization Practices.* The 2003 sample was analyzed for appropriateness of PEP because it was more representative than the 2002 sample. Stepwise syntax was created in SPSS utilizing 3 key decision variables and the *2004 Virginia Rabies Control Guidelines* Algorithm for PEP decisions to determine appropriateness of PEP.

Results: The 2002 and 2003 sample consisted of 838 PEP records, (73.6%) of 1139 PEP reported to the Division of Zoonotic and Environmental Epidemiology (central office of the Virginia Department of Health). Most PEP patients were young (mean 32.3 years) and had true exposures during spring or summer that resulted from approaching and handling a potentially rabid animal. Over half of the source animals were not captured. For the analysis of appropriateness, 55.2% (270/489) of PEP was appropriate, 22.5% (110/489) was inappropriate and 22.3% (109/489) of PEP had missing data on key decision variables. Inappropriate PEP primarily resulted from not true exposures [79% (87/110)]. Group exposures represented 42% more inappropriate PEP than individual exposures.

Conclusion: Much PEP could be avoided in Virginia if more source animals were captured. The majority of inappropriate PEP occurred because PEP was given for exposures that were not true. New educational strategies for health care providers, public health personnel and the public are recommended to reduce the number of inappropriate PEP. Standardization of data collection methods, linking human and source animal data, computerization and formation of a central database are recommended to improve human rabies PEP surveillance in Virginia

Introduction

Infection with the rabies virus can lead to encephalitis and death in humans. In the United States, rabies is a rare human disease. Although it is considered invariably fatal once symptoms develop, six recoveries from rabies infection have been reported, three in the United States.[1] Most recently, in 2004, a 15 year old female developed symptoms of rabies after being bitten by a rabid bat and became the first unvaccinated patient documented to recover from clinical rabies infection.[1] Rabies can be prevented if postexposure prophylaxis (PEP) is given in a timely and appropriate manner.[2-3] Careful evaluation of rabies exposures and appropriate decisions about human rabies postexposure prophylaxis (PEP) treatment are critical not only to the prevention of human rabies fatalities but also to avoid unnecessary administration of rabies PEP to those not truly exposed. Local health departments, health care providers and especially ED physicians must have ready access to and a working knowledge of the guidelines for rabies postexposure prophylaxis described in the *1999 Recommendations of the Advisory Committee on Immunization Practices (ACIP)* to make appropriate decisions about administration of PEP.[3] Effective communication between health care providers and rabies experts at local and state health departments is necessary for accurate initial assessment of rabies exposures, assurance that exposing animals are properly managed, and appropriate and timely decisions to administer PEP or avoidance of unnecessary PEP.[3-6] The PEP treatment regimen requires a previously unvaccinated (rabies naïve) exposed person to receive Human Rabies Immune Globulin (HRIG) injections (20 IU/kg) in and around the wound site on day 0 and to receive five intramuscular injections of rabies vaccine (days 0, 3, 7, 14 and 28).[3] Previously vaccinated persons (those that have received preexposure or postexposure regimens of Human Diploid Cell Vaccine (HDCV), Rabies Vaccine Adsorbed (RVA) or Purified Chick Embryo Cell Vaccine (PCEC) or have a

documented rabies titer) receive two IM doses of rabies vaccine (Day 0, and Day 3) after an exposure.[3]

Human rabies PEP is expensive, time-consuming, labor intensive, carries risk for adverse reactions and rabies biologics are often in short supply.[3-4, 7-8] In the United States, an estimated 40,000 people receive rabies PEP annually at a 1998 estimated per-patient cost range of $1,038 to 4,447 for a complete PEP regimen including physician and emergency department (ED) charges.[2,9-11] The first treatment is the most expensive part of the regimen, because both HRIG and rabies vaccine are given, emphasizing the importance of evaluating exposures carefully and treating appropriately when the patient is first presented for medical attention.[8-10]

On April 2, 2004 Aventis Pasteur, producer of IMOVAX® Rabies Human Diploid Cell Vaccine (HDCV) and one of only two pharmaceutical companies producing rabies vaccine for the United States issued a recall of several lots of their rabies vaccine and later halted production and distribution entirely, leaving only one manufacturer, Chiron, to supply rabies vaccine internationally.[12] The prospective for a limited supply of rabies vaccine further emphasizes the importance of evaluating each potential rabies exposure carefully and appropriately administering PEP according to the *1999 Recommendations of the Advisory Committee on Immunization Practices (ACIP)* guidelines.[3]

Virginia's *Regulations for Disease Reporting and Control*, as of July 2004, requires physicians and directors of medical care facilities to report human rabies postexposure prophylaxis to local health departments within three days.[13-14] Local health departments (LHDs) in Virginia reported to the Office of Epidemiology of the Virginia Department of Health that 586 courses of PEP were given in 2002 and 553 courses were given in 2003 by the LHDs or by private health care providers (Suzanne R. Jenkins, September 2004). PEP is indicated, according

to the 1999 ACIP recommendations and *2004 Virginia Rabies Control Guidelines*, when a human is potentially exposed to rabies virus in any of the following circumstances defined as a true exposure: "any bite, scratch or other situation where saliva or central nervous system (CNS) tissue of a potentially rabid animal [that is not available for testing] enters an open, fresh wound or comes in contact with a mucous membrane by entering the eye, mouth or nose."[3,15] Touching or handling of a potentially rabid animal or an animal or inanimate object that had contact with a rabid animal does not constitute a true exposure and is a questionable exposure unless wet saliva or CNS material from the rabid animal enters a fresh, open wound or contacts a mucous membrane.[15] Evaluation of potential rabies exposures resulting from bats is more difficult than terrestrial mammals because transmission of rabies from rabid bats to humans can occur with little historical evidence of exposure. Bites from the tiny teeth of bats inflict such minor tissue damage that they may easily go unnoticed making exposure documentation particularly problematic.[3] According to the 1999 ACIP recommendations for bat exposures,

> Rabies postexposure prophylaxis is recommended for all persons with bite, scratch, or mucous membrane exposure to a bat, unless the bat is available for testing and is negative for evidence of rabies. Postexposure prophylaxis might be appropriate even if a bite, scratch, or mucous membrane exposure is not apparent when there is reasonable probability that such exposure might have occurred. Postexposure should be considered when direct contact between a human and a bat has occurred, unless the exposed person can be certain a bite, scratch, or mucous membrane exposure did not occur. In instances in which a bat is found indoors and there is no history of bat-human contact, the likely effectiveness of postexposure prophylaxis must be balanced against the low risk such exposures appear to present. In this setting, postexposure prophylaxis can be considered

> for persons who were n the same room as the bat and who might be unaware that a bite or direct contact had occurred (e.g., a sleeping person awakens to find a bat in the room or an adult witnesses a bat in the room with a previously unattended child, mentally disabled person or intoxicated person) and rabies cannot be ruled out by testing the bat. Postexposure prophylaxis would not be warranted for other household members. (p. 9) [3]

Rabies virus is enzootic in certain Virginia wildlife species and human exposures to confirmed or potentially rabid animals continue to occur on a regular basis.[16] In 2003, 542 cases of animal rabies were reported in Virginia, 90% in wild animals (raccoons, skunks, bats and foxes) and 10% in domestic animals (cats, dogs and cattle).[16] Species are categorized as high risk or low risk based upon the incidence of rabies infection in the species and what is known about rabies transmission to humans in the particular species. In Virginia high risk wildlife species include foxes, skunks, raccoons, groundhogs or woodchucks, bats, beavers and opossums, and these animals are considered rabid unless proven negative by laboratory testing.[15]

PEP is indicated within the first 24 hours following a true exposure to a high risk wildlife species that is unavailable for testing.[3,16] It is appropriate to delay PEP for several days after a true exposure to a high risk domestic species (dogs, cats and ferrets) pending capture of the animal. PEP is indicated if the source animal remains uncaptured (stray) the third day after exposure.[16] Dogs, cats or ferrets that are collected and initially appear normal are confined for ten days to observe for signs of rabies.[16] If during the ten day confinement the animal sickens or dies, escapes, is euthanized or tests positive for rabies then PEP becomes appropriate.[16] Wild animal hybrids, the offspring of wild animals crossbred to domestic species (cats or dogs), are considered wild animals by the National Association of State and Public Health Veterinarians (NASPHV) and the Council of State and Territorial Epidemiologists (CSTE).[3] The ACIP

recommends that postexposure management for those animals be the same as for wild animals.[3] Wild animal hybrids have unknown incubation periods for rabies, unknown duration of rabies virus shedding and rabies vaccines are not licensed for use in these animals.[3] Wolf hybrids are more commonly encountered than other wild animal hybrids in Virginia. Virginia follows the recommendations of the *2005 Compendium of Animal Rabies Prevention and Control* regarding PEP for bites by wolf hybrids, e.g. it is determined on a case by case basis.[2] Euthanasia and testing of wolf hybrids that bite humans is pursued if victims and their physicians request it.

Low risk animal species in Virginia include small rodents, rabbits, squirrels and non-human primates among wild species and cattle, horses, goats, sheep, pigs and humans among domestic species. Low risk species are not considered a risk for rabies transmission unless their behavior is abnormal or aggressive or they are confirmed rabid.[15]

Beginning in 1980 more immunogenic modern cell culture rabies vaccines with fewer side effects than the duck embryo vaccine were introduced in the United States (Merieux HDCV in June 1980 and Chiron Purified Chick Embryo Cell vaccine (PCECV) FDA approved for use in 1997).[4,17] Several studies both internationally and in the United States investigated the epidemiology and appropriateness of human rabies PEP after the introduction of these new vaccines.[4-7,18-25] A pilot program for the Merieux HDVC vaccine licensed in June1980 expanded into a large, multi-state surveillance of PEP.[4] Helmick, in a twenty-one state (1980 -1981) descriptive surveillance study of 5,654 PEP cases in civilian populations, determined that when state health departments were involved in decision-making and administration using exposure definitions similar to ACIP guidelines, PEP was started and given appropriately to 88% of the persons.[3-4] Only states with 80% estimated completeness of reporting of HDCV PEP were included in the study. Helmick found that states with a long history of consultation between

state health departments and physicians (Georgia and Illinois) had a lower incidence of PEP than most other comparable states when classified by similar rabid species.[4] In the Helmick study, wild animal exposures represented only 33% of PEP given, yet represented 87% of proven rabid animals, and domestic animal exposures (dogs and cats) overrepresented PEP given in relation to their small role in animal rabies.[4] According to Helmick, 40% of PEP resulted from non-bite exposures, many part of large group exposures to a single animal; PEP that might have been avoided with more careful interviewing.[4]

A 1982 – 1983 descriptive epidemiological study of the raccoon rabies epizootic in Middle Atlantic States (Virginia, Maryland, and District of Columbia), a collaboration between local health departments and the CDC, concluded that of 133 persons who received rabies PEP resulting from exposure to wild animals (raccoons, foxes or skunks), 50% received PEP for questionable exposures.[18] Questionable exposures included touching rabid or potentially rabid animals and indirect contact through handling fomites or an animal that had contact with a rabid animal, exposures considered (then and now) to convey minimal or no risk according to ACIP guidelines.[3,18] This study was limited by possible non-response and selection bias. Sampling was not random but voluntary, and over 98% of the data from the study was limited to six counties and one city, although 22 counties and cities were queried.[18] Data sources retrieved through personal accounts and retrospective review of records were often incomplete, inconsistent and may have introduced recall bias.[18]

A 4000% increase in human rabies PEP in New York, from 81 cases in 1989 to 3,336 cases in 1993, has been attributed to the spread of the Mid-Atlantic raccoon rabies epizootic into New York in 1990.[24] Rabid animals increased in New York from 54 in 1989 to 2746 (89% raccoons) in 1993.[24] In response to these analyses and the Healthy People 2000 objective to reduce by 50%

the need for human rabies PEP by the year 2000, an epidemiological study was conducted of all human rabies PEP reported in four upstate New York counties, 1993 and 1994.[24, 26] Of 1,173 cases of PEP reported, 70% (817) resulted from non-bite exposures, predominantly indirect exposure to saliva on animal or fomites.[24]

A telephone survey of 28 local Kentucky health departments that reviewed PEP patient records, found that of 97 patients that received PEP in 1994, 18 (18.6%) of the exposures were from scratches, licks or other non-bite exposures, 71 (73.2%) exposures resulted from bites and 8 (8.2%) were unknown. Domestic animal exposures represented 80 (82.5%) of the 97 PEP treatments.[23] The researchers found that 83 (77.1%) of the animals were not available for observation and testing and concluded that the incidents were not appropriately handled and laws were not followed.[23] A major limitation of the Kentucky study was that many records were incomplete and lacked enough detail for variable analysis.[23]

Moran et al. conducted a prospective case series study of 2030 animal exposure patient presentations at 11 urban university EDs from July 1996 to September 1998.[19] Moran et al. found, using the 1999 ACIP guidelines, that of 136 PEP treatments, 54 (40%) PEP treatments were given inappropriately indicating inappropriate case management.[19] Although rabies in domestic animals is now rare and 90% of animal rabies in the United States occurs in wildlife, in this study dog and cat exposures represented 86% of all PEP given and most of the inappropriate PEP.[19] Of 60 cases that reported no consultation with local health departments, 16 (27%) of PEP treatments were determined inappropriate and of eight cases reporting consultation, two (25%) of PEP were inappropriate.[19] Moran concluded that the best way to reduce inappropriate PEP is to increase the proportion of source animals that are observed and tested. Moran also concluded

that medical health providers may immediately administer PEP if they are not confident that the animal will be collected.[19]

A Florida study, a retrospective review of 160 PEP patient medical records from 22 county health departments (July through September in both 1997 and 1998) randomly selected from 67 county health departments, revealed that decisions about PEP administration were appropriate for 104 of 146 cases (71%), inappropriate for 32 of 146 cases (22%) and 10 of 146 (7%) resulted from out of state decisions.[5] This study excluded 14/160 (9%) of PEP for missing information prior to PEP appropriate analysis.[5] Using the 1999 ACIP guidelines, the Florida researchers concluded that among 32 cases of inappropriate PEP, 15 PEP cases had no documented rabies exposure (*possible exposure* or *touched animal*) and 7 cases were exposed to animals that tested negative for rabies. Of the 10 remaining cases, 8 PEP were given in lieu of observation and testing even though source animals were available and 2 PEP resulted from exposure to low risk species.[5] Multiple or group exposures resulted in a substantial proportion of inappropriate PEP indicating the need for health care providers and public health staff to pay special attention to assessment of exposures in these situations.[4-5, 22]

Human rabies is rare in the United States because of effective rabies prevention practices and treatment, 53 cases of human rabies have occurred since 1980.[1,27-33] In the United States, human rabies fatalities occur primarily due to failure to seek effective PEP because of unrecognized or unsuspected exposures.[33-35] Cryptic cases of rabies, no documentation of rabies exposure even with a thorough history, have resulted in the majority of recent human rabies cases in the United States.[35] According to Messenger, Smith and Rupprecht, since 1958, 63% of 70 cases in 1958-2001 had no documentation of a bite from a rabid animal.[35] Postexposure prophylaxis, including all components (wound treatment, HRIG and rabies vaccination), is consistently effective in

preventing rabies virus infection mortality if exposure is suspected .[3, 35] Two cases of human rabies have been reported in Virginia in the last 52 years of reporting. A 29-year-old male residing at Nottoway Correctional Center died of insectivorous bat variant rabies in 1998, without any history of exposure to the bite or scratch of an animal.[33] In 2003, a 25-year-old man from northern Virginia died from southeastern raccoon rabies virus variant also without history of a potential rabies exposure.[30]

The Centers for Disease Control and Prevention surveillance data indicate that over the last one hundred years the principal reservoir hosts for rabies in the United States have changed significantly. Prior to 1960 rabies primarily occurred in domestic animals; today 90% of rabies occurs in wild carnivores and bats.[11] There is an emerging pattern of human rabies deaths resulting from bat exposures in the United States.[34-35] Since 1990, of 35 cases of human rabies indigenous to the United States, 33 (94%) have resulted from bat variant rabies virus.[28-33] Some bat species appear to transmit rabies more readily than other animal species and assessment of bat exposures is particularly problematic.[16,34] Specifically two bat species, *Lasionycteris noctivagans* and *Pipistrellus subflavus,* are linked with rabies virus variants that have accounted for more than 70% of human cases and 75% of deaths due to unrecognized exposures in the United States.[34-35]

In Virginia the last descriptive study of the epidemiology of human rabies postexposure prophylaxis (PEP) was twenty years ago, 1982 -1983.[18] A surveillance study with current data on PEP patient demographics and types of exposures, circumstances and source animal factors that lead to PEP is long overdue in Virginia and is indicated in light of the changing epidemiology of rabies, the variable epidemiology between regions of the United States, the emergence of new reservoir hosts and recognition of more virulent rabies virus variants.[34-36] Evidence-based

information about the epidemiology of human rabies PEP in Virginia is necessary to develop appropriate education for health care providers, public health practitioners and the public. These data should be evaluated with reference to recent and future surveillance data across the United States; events in other regions may portend an emerging situation or a future trend in Virginia.[35] Limited supplies of rabies vaccine and HRIG and expensive, unpleasant vaccine regimens emphasize the need to evaluate evidence-based data to improve the methods of assessment of exposures for appropriate administration of PEP in Virginia. The purpose of this descriptive study is to characterize a sample population that received human rabies postexposure prophylaxis (PEP) in Virginia as a result of exposures in 2002 and 2003. We specifically want to determine the types of exposures and circumstances that resulted in PEP in this sample population. Using the *2004 Virginia Rabies Control Guidelines and 1999 Recommendations of the Advisory Committee on Immunization Practices (ACIP)* guidelines, we will determine to what extent rabies postexposure prophylaxis was administered appropriately in Virginia.[3,15]

Objectives

The primary objective of this descriptive study is to answer the question "Is human rabies postexposure prophylaxis being administered appropriately in Virginia according to the *2004 Virginia Rabies Control Guidelines* and the *1999 Recommendations of the Advisory Committee on Immunization Practices (ACIP)*?" This study will also characterize the population that received human rabies PEP and determine the types of exposures and circumstances of exposure that led to human rabies postexposure prophylaxis in Virginia.

The results and recommendations from this study will help the Virginia Department of Health (VDH) evaluate the administration of PEP in Virginia and target recommendations on appropriate PEP administration to health care professionals and public health personnel. The information from this study will also help the Virginia Department of Health evaluate current PEP data collection methods at Virginia local and district health departments and make recommendations for standardization of data collection. The results of this study may have application for evaluating human rabies postexposure prophylaxis nationally.

Methods

Definition of Study Sample

The data used for this retrospective descriptive study was a convenience sample of patient records and animal exposure reports from 838 PEP patients exposed to either potentially rabid or rabid animals or humans during calendar years 2002 and 2003. PEP patients included in the sample must have begun a course of human rabies postexposure prophylaxis treatment or received at least one PEP treatment in Virginia that was reported to a Virginia health district. Persons that refused recommended PEP treatment were excluded from this study. All existing 2002 and 2003 PEP patient and source animal computerized and paper record surveillance data (demographics, animal exposure factors, PEP characteristics, and source animal factors) were requested from 35 Virginia health districts within 5 regions. Virginia health district directors are requested by the Division of Zoonotic and Environmental Epidemiology (DZEE), within the central office of the Virginia Department of Health, to annually report aggregate numbers of PEP that have been reported to or administered by the local health departments throughout the year. PEP reported may be part of the full rabies naïve regimen or the two injection regimen given to previously vaccinated persons. For the 2002 study sample, 19 of 35 health districts (54%) provided PEP data on 59% (344/586) of PEP cases reported to the DZEE. For the study 2003 sample, 24 of 35 health districts (69%) provided PEP data on 89% (494/553) of PEP cases reported to the DZEE. Expedited Institutional Review Board (IRB) approval was received from both Virginia Commonwealth University and Virginia Department of Health (VDH).

Existing computerized or paper record PEP data were both reviewed and extracted at the Virginia Department of Health offices in Richmond, Virginia or directly at Virginia health district offices between August 30, 2004 and December 10, 2004. PEP patient records included

Virginia Department of Health Confidential Morbidity Reports (EPI 1 forms) and patient health records from Virginia health departments. Source animal records included VDH environmental health animal exposure reports and locally administered computerized files.

Definition of Study Variables

The outcome variable for this study was human rabies postexposure prophylaxis (PEP), administered in Virginia as a result of potential exposure to rabies during calendar years 2002 or 2003, and reported to Virginia health districts. Included in the analyses were all patients that were known to have received at least part of a course of PEP in Virginia, regardless of the geographic area in which the exposure occurred.

Data were collected in the following categories: demographics, exposure factors, source animal factors, and PEP factors. A data collection instrument was created and utilized as a guide for systematic extraction and recording of variables associated with human rabies PEP (Appendix A). Data collected on patient demographics included county/city of residence, age, gender, race, ethnicity and occupation. Patient exposure factor data included date of exposure, county/city, type, circumstance, associated activity, related occupation and anatomical site. Source animal factor data included species, availability for observation or testing, date of collection, ownership status, rabies vaccination status, behavior and health, exposure to confirmed or suspected rabid animal, number of persons and animals exposed to source animal, rabies direct fluorescent antibody test results and outcome of confinement and observation of source animal. Human rabies PEP factors collected were: date PEP initiated, patient's previous rabies vaccination history, whether PEP was completed, local adverse reactions, general systemic adverse reactions, central nervous system reactions, peripheral nervous system reactions and immune complex-like reactions.

Several demographic variables were recoded for clarity and to facilitate statistical analyses. City/county of residence and exposure were recoded into federal information processing standards codes (FIPS codes), a standardized set of numeric codes issued by the National Institute of Standards and Technology (NIST) to ensure uniform identification of geographic entities through all federal government agencies.[37] Virginia health districts were recoded into their geographical regions: Northwest, Northern, Southwest, Central and Eastern. Age was analyzed as a continuous variable (mean, median, standard deviation, minimum and maximum), recoded into 5-year age categories and into child (< 18 years old) and adult (>17 years old) categories to calculate age-specific rates of PEP by district and regions based on the 2002 Virginia population VDH Health Statistics.[38]

Patient exposure and source animal variables were recoded for analyses. Type of exposure was recoded into true exposure or not true exposure categories according to rabies exposure definitions for appropriate PEP decisions in the *2004 Virginia Rabies Control Guidelines* and the 1999 ACIP recommendations.[3, 15] True exposures were defined using the *2004 Virginia Rabies Control Guidelines*, "Any bite, scratch or other situation where saliva or central nervous system (CNS) tissue of a potentially rabid animal enters an open, fresh wound or comes in contact with a mucous membrane by entering the eye, mouth, or nose", and the 1999 ACIP definitions including the recommendations for potential bat exposures, described earlier.[3, 15] True exposures included bites, saliva on mucous membranes, saliva in an open wound, potential (suspect) bat exposures, and exposure to body fluids (where exposure to CNS material or saliva could not be ruled out) on mucous membrane or in an open wound. Some districts combined exposures to saliva, CNS material, blood, urine and feces into one *body fluid* category when exposure to saliva and/or CNS material could not be ruled out. Not true exposures included exposure to: saliva or

body fluids (CNS material, saliva, urine, feces or blood) with no mucous membrane or open wound contact; scratches; touching an animal; and secondary exposures. “Secondary exposures” refer to exposure to a fomite or animal that had contact with a potentially rabid animal. Multiple response variables (type of exposure, anatomical site of exposure and source animal behavior/health) were prioritized into a single primary response for analysis. If multiple types of exposures were indicated for a PEP patient, then the true exposure (as defined by the *2004 VA Rabies Control Guidelines* and 1999 ACIP recommendations) became the primary type of exposure.[3,15] If multiple anatomic sites of exposure were indicated for a PEP patient, then the single site closest to the central nervous system (brain, then spinal cord) became the primary anatomical site of exposure. Behavior/health categories were collapsed into the following primary behavior categories (aggressive, injured, sick, neurological signs, hypersalivation, dead, overly friendly and normal). Source animal species were recoded into wild and domestic species and high and low risk species (risk for transmission of rabies to humans in Virginia), according to the *2004 Virginia Rabies Control Guidelines*.[15] Domestic animals designated as stray indicated no ownership and included feral (breeding in wild) domestic animals. Confinement status was recoded into released normal (domestic dog or cat normal and healthy after ten days of observation) or sickened and died (including euthanized, escaped with incomplete confinement, and tested positive for rabies during confinement). A captured variable was created to include all animals collected for either rabies testing or confinement. Dogs, cats and ferrets were recoded into a variable for analysis. An ‘over 2 day’ variable, used for wild species, was created to designate rabies test results that would be received after 48 hours of patient exposure. A rabies positive variable was created to include source animals that sickened and died during confinement as well as animals with positive or unsatisfactory rabies direct fluorescent antibody

test results. A group exposure variable was created to characterize PEP patients as part of a group exposure (>1 person exposed to 1 animal) or individual exposure (1 person exposed to 1 animal) and to look at proportions of group and individual exposures that resulted in PEP.

Appropriateness of PEP

To answer the question "Was PEP administered appropriately in Virginia?" we referred to the *1999 Recommendations of the Advisory Committee on Immunization Practices (ACIP)* exposure criteria and used Figure 1: The Virginia Department of Health Algorithm for Human Pre- and Post- Exposure Treatment in the *2004 Virginia Rabies Control Guidelines*.[3, 15] PEP resulting from human and wolf hybrid exposures were excluded from PEP appropriate analysis because in Virginia they are considered on a case-by case basis.

Statistical Analysis

All data collected from existing computer data files and existing paper records of PEP patients were entered into a Microsoft Excel file. Personal identifying information was not recorded. The human rabies PEP 2002 and 2003 Excel data file was exported to SPSS 12.0. Crude and age-specific PEP incidence rates were calculated for districts and regions using MS Excel and 2002 Virginia population VDH Health Statistics.[38] ArcGIS 9, ESRI GIS Mapping and Software was utilized for geographical mapping of crude and age-specific incidence rates by region and to show the distribution of districts that provided data by region. Microsoft Excel and Microsoft Word were used for graphics and tables.

The PEP sample population was characterized by demographic, exposure, source animal and human rabies PEP factors by calculating frequencies, percentages and performing cross tabulations for 2002, 2003 and both years combined. Total percentages were most representative

for description of the PEP study sample because many variables had large percentages of unknown or missing information. One rabid human was excluded from source animal analysis.

For the appropriateness of PEP analysis, 2003 PEP data was most representative. Data collected from 2002 were excluded from analysis because of inconsistencies. In this study, several districts had large discrepancies between the number of PEP reported to the DZEE in 2002 and the number of PEP data provided to the study for that year. In 2003 several health districts began more efficient electronic collection of human rabies PEP data because of the implementation of software for environmental health programs to use in their rabies control programs. This resulted in more data being stored and made available in 2003 than in 2002.

Appropriateness of PEP decisions was determined using SPSS 12.0 to create stepwise syntax and a new recoded variable for each key decision pathway ("true exposure?", "captured?" and "rabies positive?") in the *2004 Virginia Rabies Control Guidelines* Algorithm for Postexposure Treatment (Figure 1). An objective variable "PEP appropriate?" was built and defined with syntax at each level of the PEP decision algorithm and SPSS gathered those PEP that met the criteria for appropriateness of PEP to ultimately answer the question, "Was PEP administered appropriately?", for each PEP patient. Differences in the distributions of proportions among inappropriate and appropriate PEP by factors were tested using Pearson's chi-square test for proportions and p-values were analyzed at the = 0.05 significance level.

Results

Sample Characteristics

For this study, 838 PEP patient records were collected and analyzed, 73.6% of 1139 of the total PEP reported to the DZEE in 2002 and 2003 (Table 1). The data collection period was defined by patient exposures that occurred between January 1, 2002 and December 31, 2003. The number and percentages of Virginia health districts that provided data to this study and PEP records reported and provided by region for 2002 and 2003 are displayed in Table 1. There were inconsistencies between data reported by districts to the DZEE and data provided to the study, especially in 2002. Some districts that provided PEP data for a particular year had not reported any PEP to the DZEE and others that reported PEP for a particular year did not provide data to the study. In 2002, 3 districts (1 each in the Northern, Southwest, and Eastern regions) and for 2003, 4 districts (1 each in the Northern and Central and 2 in the Eastern regions) neither reported data nor provided data to the study. These 7 districts were included as districts not providing data to the study in Table 1. In 2002, 54% (19/35), and in 2003, 69% (24/35), of Virginia health districts provided data, patient PEP records and animal exposure reports, resulting in the study sample of 838 PEP for review. Regions varied by year with respect to the proportion of districts that provided PEP data to the study, from 33% (3/9) districts in the Eastern in 2002 to 80% (4/5) of districts in the Northern (2003) and Northwest (2002 and 2003) regions. Table 1 shows that districts provided records on less than 60% (344/586) of PEP cases reported to the DZEE in 2002 (ranging from 43% to 70%), whereas districts provided about 90% (494/553) of PEP reported in 2003 (ranging from 73% to 131%). The Eastern region is of interest, because it had the lowest district response rates for both years, 3/9 districts provided

data in 2002 and 5/9 in 2003, yet for 2003, 31% more PEP cases were provided to the study than were reported to the DZEE in 2003.

To examine the geographic distribution of PEP provided to this study in 2003, PEP rates for those districts that provided data to the study were calculated but are displayed by region for reasons of confidentiality (Table 2 and Figures 2a - d). Within regions, the distribution of urban versus rural districts that did and did not provide PEP was similar; therefore, we feel that these rates can be used to indicate where PEP was administered more frequently (Figure 2a). Displayed in Table 2 and Figures 2b – d are the estimated annual crude and age-specific incidence rates of PEP by region for the 2003 sample. The crude PEP incidence rate for the entire study area was $9.3/10^5$/yr. The PEP rate for children ($10.3/10^5$/yr) was 32% higher than for adults ($7.8/10^5$/yr). The highest rates of PEP were in the Northwest ($15.1/10^5$/yr) region followed by the Southwest ($12.4/10^5$/yr) and Eastern ($10.0/10^5$/yr) regions. Within both the Northwest and Southwest regions, the PEP rate for children was 70% greater than the rate for adults. The Central and Northern regions, of predominantly urban geography, had the lowest rates of PEP, $5.3/10^5$/yr and $6.0/10^5$/yr PEP, respectively.

Demographic Characteristics

Demographic characteristics of those who received PEP are displayed in Table 3. Total percentages are presented for those variables with over 5% missing information. The mean and median age of the 2002 and 2003 sample was 32.3 and 31.0 years, respectively, with an age distribution from 2 months to 97 years. Number and percentage of infant, child and adult PEP by age are shown in Table 3. Figure 3, percent PEP and percent 2002 Virginia population by five-year age categories, displays a bimodal distribution in percent PEP with two age-group peaks occurring at 5 – 19 years and 30 – 39 years that do not follow the 2002 Virginia population trend.

The proportion of PEP patients steadily increased through childhood from 6.5% for those 0 – 4 years to peak at 9.4% for 15 – 19 year-olds. During young adulthood (20 – 29 years) PEP dropped to about 6.5%, and peaked again to about 9.6% between 30 - 34 years after which there was a steady decrease in PEP patients to a low of 1.1% after 65 years. Gender distribution shows a slightly greater proportion of females than males received PEP in 2002 and 2003 (Table 3). Data on race and ethnicity were missing from 57.4% and 69.9%, respectively, of patient records.

Exposure Characteristics

Animal exposures resulted in PEP throughout every month of both 2002 and 2003 but showed a seasonal distribution (Figure 4). PEP numbers increased in the spring and summer months for both 2002 and 2003 to peak in July, with a second peak in late fall, primarily because of increases in 2003. PEP numbers were lowest in January.

Types of exposure that resulted in PEP, categorized as true or not true, are shown in Table 4. Total percentages are presented for those variables with over 5% missing information. True exposures meet the 2004 VDH Guidelines and the 1999 ACIP recommendations for PEP, "any bite, scratch or other situation where saliva or central nervous system tissue of a potentially rabid animal enters an open, fresh wound or comes in contact with a mucous membrane by entering the eye, mouth, or nose."[15] True exposures, that met the 2004 VDH Guidelines and the 1999 ACIP recommendations for PEP treatment, resulted in the majority of patient PEP in the study. Among 838 PEP exposures, 66.7% (559/838) were categorized as true, 17.8% (149/838) were not true and exposure type was unknown for 15.5% (130/838). Table 4 shows that 57% (478/838) of PEP resulted from animal bites and 5.5% (46/838) of PEP were from suspect bat exposures. There were differences between 2002 and 2003 data with respect to number and percentage of PEP resulting from saliva or body fluid on mucous membranes or in open wounds

and secondary exposures. Not true exposures (types of exposures that do not require PEP) resulted primarily from touching animals, secondary exposures and scratches. Figure 5a shows that among 559 PEP that were true exposures, the majority, were due to bites, 85.5% (478/559), and suspect bat exposures, 8.2% (46/559). Among 149 PEP that were not true exposures, 31.5% (47/149) resulted from touching animals, 26.2% (39/149) from secondary exposures, and 24.2% (36/149) from scratches (Figure 5b).

Data on both circumstance of exposure and activity leading to exposure were missing from over 50% of PEP patient records and the distribution of these exposures by category varied between 2002 and 2003. But the available data for these two characteristics shows that the primary circumstance leading to exposure and PEP was the victim approaching the source animal, resulting in 59.0% (220/373) of PEP. Handling the source animals resulted in 44.6% (161/361) of PEP for activity leading to exposure and *other* activities (exposure to a fomite or animal that had contact with a potentially rabid animal or a potential bat exposure) led to 26.0% (94/361) of the PEP. In about 21% of both circumstances and activities that led to PEP the source animal approached (81/373) or attacked (76/361). Approximately 54% (449/838) of PEP cases had data available on primary anatomic site of exposure, and for those data collected, 66.8% (300/449), of victims were exposed on the upper limb (arm, hand, finger or thumb).

Overall, individual exposures (1 person to one source animal) represented the majority, 63.6% (533/838), of PEP, group exposures (>1 person exposed to one source animal) represented 30.7% (257/838) of PEP, and information was missing for 5.7% (48/838) of PEP (Table 4). The 257 PEP patients with group exposures represented 62 source animals. The group size ranged from 25 groups of 2 persons to a single group of twenty-three persons exposed. Overall 593 source animals exposed 788 PEP patients in the sample (excluding 1 human with rabies).

Source Animal Characteristics

Table 5 displays characteristics of 593 source animals representing 788 PEP in our sample. Total percentages are presented for those variables with over 5% missing information. Among 571 source animals in the sample, 72.2% (412/571) were domestic species, excluding 1 human, primarily cats 50.7% (209/412) and dogs 47.8% (197/412). Wild species represented 27.8% (159/571) of the source animals, of those 41.5% (66/159) were raccoons and 27% (43/159) were bats. Species information was missing on 3.7% of source animals. Source animals in this study were twice as likely not to be captured as captured. About 57% (337/593) of source animals in our sample were not captured for observation and/or testing for rabies. For 13.7% (81/593) of the source animals, information was missing on capture. Among those captured, 76.5% (130/170) were positive for rabies (Table 5). For animals found to be rabies positive, primary behavior information was missing on over 50% (70/130). Of those with behavior recorded, aggression was seen in 63% (38/60) and 25% (15/60) appeared sick (Table 5).

Table 6 displays species of source animal captured by rabies status and number and percent of animals and PEP administered. The ratio of PEP to animal is also displayed by rabies status and source animal species (Table 6). Among captured animals that tested positive for rabies, domestic animals represented 45% (58/129), whereas among captured animals that tested negative, 84% (32/38) were domestic. For domestics, 64% (58/90) tested positive. Among cats and dogs tested, 77% (44/57) and 40% (12/30) were positive, respectively. Captured wild species were more likely to test positive than negative, 92.2% (71/ 77 tested). Overall among animals that tested rabies positive, domestic species resulted in more PEP per animal exposure than wild, 2.8 and 1.7 PEP per animal, respectively. For rabies negative animals, the PEP to animal ratio was similar for both domestics and wild, 1.2 and 1.5, respectively (Table 6).

Rabies vaccination status was missing from 88% (361/412) of domestic animals in the study. For those 51 animals with data available, 17 were current or had ever been vaccinated.

Appropriateness of PEP

Data from the 2003 sample (n = 494) were analyzed using the *2004 Virginia Rabies Control Guidelines Algorithm* for Postexposure Treatment (Figure 1) and the 1999 ACIP recommendations to determine the appropriateness of PEP decisions. Only 2003 data were analyzed because the external and internal validity of the data from 2002 was questioned since the numbers of 2002 PEP provided by districts to the study varied markedly from those reported to the DZEE in 2002. PEP resulting from human and wolf hybrid exposures (n = 5) were excluded from analyses because they are evaluated on a case-by-case basis in Virginia. For the 2003 sample, PEP was administered appropriately 55.2% (270/489) of the time, inappropriately 22.5% (110/489) of the time, and appropriateness of PEP could not be determined for 22.3% (109/489) of PEP because of missing data (Figure 6).

Table 7 compares the number and percent of inappropriate and appropriate PEP by patient demographic and exposure characteristics. There were significant differences in the distributions of proportions for type of exposure, number in exposure group, and region of exposure. The majority of inappropriate PEP, 79% (87/110), resulted from not true exposures (touching animals, secondary exposures, scratches and exposure to body fluids with no mucous membrane or open wound contact). True exposures resulted in 21% (23/110) of inappropriate PEP because of exposures to rabies negative animals. Most patients that received inappropriate PEP had group exposures, 59% (64/110). The proportion of inappropriate PEP was 42% greater for those persons with group exposures compared to those with individual exposures.

Table 7 shows that the proportions of inappropriate PEP varied by geographic region of exposure. Among the five Virginia regions displayed in Table 7, the proportions of inappropriate PEP were highest for the Southwest [36% (39/110)], Northwest [29% (32/110)], and Eastern [20.9% (23/110)] regions. The Northwest and Southwest regions had 4 to 5 times greater proportions of inappropriate PEP, respectively, than the Northern and Central regions (Figure 7a). Figure 7b shows that the highest proportions of inappropriate PEP within regions occurred in the Northwest [37.6% (32/85)] and Southwest regions [38.6% (39/101)].

For the appropriateness of PEP algorithm analysis, 275 animals represented 379 PEP (Table 8). Table 8 compares the number and percent of source animals in the inappropriate and appropriate PEP groups (exposed patients that received either inappropriate or appropriate PEP) by selected factors. Total percentages are presented for those variables with over 5% missing information. Significant differences in the distribution of proportions for appropriate and inappropriate PEP were found with respect to the following source animal variables displayed in Table 8: domestic or wild species, captured, ownership status and rabies status. More than half of the source animals were domestic species for both inappropriate, 56% (33/59), and appropriate PEP 77% (166/216) PEP groups. Among inappropriate PEP, 84% (48/57) of animals were captured. Among the inappropriate PEP group of animals, 32% (18/56) were owned and 53% (26/49) of animals that were captured tested positive for rabies.

Discussion and Conclusions

This study was the first in over twenty years to describe types and circumstances of animal exposures as well as source animal characteristics that resulted in administration of PEP and to evaluate the appropriateness of human rabies postexposure prophylaxis decisions in Virginia. The results of this study provide the Virginia Department of Health a baseline summary of PEP surveillance data for 2002 and 2003 on patient demographic, exposure and source animal factors. This information will facilitate the evaluation of PEP treatment decisions (past, present and future), help target recommendations on appropriate PEP administration to health care professionals and public health officials, and help target informational interventions on human behavior to prevent rabies exposures.

For the overall sample (2002 and 2003), the majority of PEP patients were young (mean 32.3 years) with the highest risk age groups for exposures and PEP between 5 and 19 years and 30 to 39 years. Most PEP patients were exposed to source animals in the warmer months of late spring and summer when people are often involved in outdoor activities. PEP usually resulted when people approached and handled the source animal or had a secondary exposure to fomites or animals exposed to the source animal. These preventable circumstances represented 259 PEP in this study that could have been avoided. These predominant circumstances of exposure are consistent with other PEP studies.[4-6,18,23-24]

The rate of PEP for children was about 30% higher than for adults for the entire geographic sample area. Within the predominantly rural Northwest and Southwest regions, the rate for children was almost double that of adults. Children may spend more time outdoors and have more opportunity to encounter potentially rabid animals in these geographic regions. Health care providers may be more inclined to administer PEP to children because of inability to acquire

accurate exposure information, parental pressure, or a systematic difference between discernment of exposures and treatment decisions between children and adults. The apprehension about rabies in children may be higher in different regions of the state because of a higher incidence of animal rabies and more opportunities for exposure to wild animals.

True exposures, primarily bites (57%), resulted in the majority of PEP in our study. Other PEP studies have reported from 16% to 73% of PEP resulted from bites.[4-5, 23] Not true exposures resulted in 18% of PEP in our study, compared to from 6% to 70%, reported by other investigators, for questionable or non-bite exposures.[5,18,23-34]

Capture of source animals and subsequent confinement and/or testing provides information essential to appropriate PEP decisions. In this study, 57% of source animals were not captured and, therefore, could not be tested for rabies or confined. Capture status was unknown for another 14%. If these 418 animals, representing 498 (59%) of the PEP in this study, had been captured for testing and/or confinement, much PEP could have been avoided. Although identification and capture of all animals may not be feasible, health care providers have a responsibility to rapidly notify animal control of exposures to potentially rabid animals to make it more likely that the animals are captured.

A number of districts provided patient PEP information to the study without matching source animal information (animal exposure reports). Although species and type of exposure were indicated on some Confidential Morbidity Reports (EPI 1 forms), animal capture and rabies status were not recorded. Capture of source animals is essential not only to determine rabies status and appropriateness of PEP, but also to remove a potential source of rabies and prevent more exposures. One rural health district director in this study received ED reports of all animal exposures and PEP within 24 hours of occurrence and this district was very effective in animal

exposure trace backs. Rabies PEP surveillance and communication between EDs and public health departments ideally could be improved through a statewide electronic database linking human exposures and PEP treatment information at EDs to source animal information at public health departments.

Once a person has a true exposure or an exposure to a potentially rabid animal, capturing the responsible source animal is the most important factor that can reduce the overall rate of PEP. Only after capture can the animal be confined and/or tested to determine rabies status. Domestic species represented the majority (72%) of source animals in our study and among the captured animals that tested negative in the study, 84% were domestic. This suggests that if all of the domestics in the study were captured and tested or confined and observed, much PEP could have been avoided.

Although 90% of animal rabies reported in Virginia in 2003 occurred in wild species, in this sample, wild species represented 55% and domestics 45% of rabid source animals captured.[16] Ninety-two percent of captured wild species in this study were positive for rabies. All raccoons, foxes and skunks captured and the majority of bats captured, about 70%, tested positive for rabies. Cats were more likely to be positive than dogs, consistent with previous findings.[39] Captured dogs were more likely to test negative. Cats were the most frequently captured domestic animal and 77% of cats tested positive in this study. Cats have more opportunity for rabies exposure than dogs; they are often free-roaming and unvaccinated. Rabies prevention education should emphasize the high likelihood of rabies in all wild species and cats, but should also warn the public not to approach any unfamiliar animals. Rabies vaccination of domestic dogs and cats continues to be the mainstay for rabies prevention in these species, yet in this study many owned cats and dogs were not routinely vaccinated against rabies.

We utilized the *2004 Virginia Rabies Control Guidelines* algorithm for PEP decisions and the 1999 ACIP recommendations for human rabies postexposure treatment to evaluate exposures and appropriateness of PEP decisions.[3,15] The *2004 Virginia Rabies Control Guidelines* recommend that Virginia public health personnel and health care providers use these references when evaluating potential rabies exposures and making decisions about PEP. In the 2003 sample of 489 PEP patients, PEP decisions were appropriate for 55% of the patients, inappropriate for 23% of the patients, and appropriateness of PEP could not be determined for 22% of patients because of missing information in records. Moran et al., in a prospective case series of urban EDs (Emergency ID Net), also followed an algorithm that was developed based on ACIP guidelines to evaluate appropriateness of PEP and found that 40% of PEP was administered inappropriately.[19] Conti et al. reported 71% appropriate PEP and 22% inappropriate PEP in a study that randomly selected Florida county health departments to review PEP records and included only those that met specific criteria.[5] A 21 state PEP surveillance study by Helmick of the newly introduced rabies human diploid cell vaccine in 1980, found that when state health departments were involved PEP was given appropriately to 88% of patients.[4]

This retrospective chart review study involved actively collecting PEP data from a passive surveillance system. All health districts that provided data to the study within the collection time frame were included in the analysis. This resulted in a convenience sample. Missing information from all PEP records provided was included in the analysis to supply information on completeness of data collection from the districts providing data to the study. By following the algorithm we were able to evaluate where data was missing at each stage of the PEP decision process. About one fourth of PEP could not be analyzed for appropriateness because of missing information on one or more of the three key decision variables: whether the type of exposure was

true or not, whether the animal was captured or not, and if the animal rabies status was positive or negative. Missing information on type of exposure and source animal rabies status, factors necessary to determine appropriateness of PEP, may result in much unnecessary PEP. However, we have no way of knowing if PEP decisions were based only on the information recorded at the health departments or if treating physicians obtained other information that did not get entered into the health department databases, forms or records reviewed. More complete and accurate data collection on type of exposure, source animal capture and rabies status is essential for health care professionals to determine if PEP is appropriate and for follow-up on exposures to potentially rabid animals. Public health professionals and health care providers have important roles in this process. Open lines of communication between health care providers and public health professionals are critical to reporting animal exposures for capture, follow-up investigations and for consultation and evaluation of exposures to avoid inappropriate PEP. Helmick found that when health care providers consulted with state health departments PEP was reduced from five to sevenfold compared to no consultation.[4] Careful and detailed history taking and documentation in patient medical records as well as in animal exposure reports are essential to determine appropriateness of PEP.

Not true exposures resulted in the majority (79%) of inappropriate PEP. The first critical step in the VDH PEP decision algorithm requires evaluation of the type of exposure, "Did the person receive contamination of an open wound or mucous membrane by saliva or brain material from a bat, dog, cat, ferret or other terrestrial mammal?" These decisions can be made with knowledge of or reference to the *2004 Virginia Rabies Control Guidelines*, the 1999 ACIP recommendations and, if necessary, consultation with a Virginia Department of Health staff member.

Why did 87 people with not true exposures in this sample receive inappropriate PEP? Several possible explanations follow: 1.) The health care provider did not know the definition of a true exposure; 2.) the documentation in the patient's record was incomplete or inaccurate because details were omitted; 3.) careful interviewing of the patient did not occur or was not possible in the case of a child or mentally challenged person; or 4.) it was unclear whether the rabid animal's body fluids actually contacted an open wound or mucous membrane on the patient. The most influential factor leading to inappropriate PEP in our study may have been that over half of the captured source animals in the inappropriate PEP group tested positive for rabies, which may have made treating physicians and patients more likely to ignore not true exposures. Rabies is 100% fatal and fear of a highly fatal disease and potential litigation may influence health care providers to over treat patients or the patient or minor patient's parent(s) may have demanded treatment. Group exposures represented about 60% of inappropriate PEP in our sample. Helmick suggested that group size may be associated with unnecessary PEP and that as the group size increased in his study that the proportion of PEP resulting from non-bite exposures increased.[4]

Group exposures represented a greater proportion of inappropriate PEP than individual exposures in our sample, although we did not see a trend with increasing group size. Psychological forces may be at work among victims of group exposures. Discussions among victims may result in exaggeration of exposures and mass panic. The lack of knowledge and understanding of what constitutes a true exposure and how rabies is transmitted may result in misconceptions about the need for treatment. Health care providers may be subjected to more pressure to begin PEP treatment when multiple persons are involved in exposures and exposure accounts are not certain or are confused. With group exposures, as in all exposures to potentially

rabid animals, it is important for health care providers to interview patients carefully and document exposures accurately to avoid unnecessary PEP.

The highest proportions of inappropriate PEP and total PEP occurred within the Southwest, Northwest, and Eastern regions of Virginia. This may be explained by the rural geography of these regions. The overall incidence of animal rabies may be higher in these regions resulting in a high perceived threat level and elevated fear of rabies resulting in more inappropriate PEP.

This study was limited by the sampling methods used. Human rabies PEP patient data collection presents challenges, many in this study were consistent with those previously described.[5,18,20,23] Our data was collected from a convenience sample, 838 patient PEP records voluntarily provided by 24 of 35 Virginia health districts. Although the 24 districts that provided data are from various regions and geographic areas, the results may not be representative of the entire state. Health districts provided PEP records that were available, a possible source of selection bias. PEP data from health districts that responded may have been systematically different (more complete and/or accurate) than data from those not responding.

We questioned the external and internal validity of the 2002 sample of data. The 2002 PEP sample had inconsistencies within several health districts between the number of PEP passively reported to the DZEE in 2002 and the number of PEP records provided to the study. These inconsistencies can to some extent be explained by weaknesses of a passive reporting system, better data collection in 2003 resulting from the implementation of software for environmental health programs to use in their rabies control programs by some districts, and possibly redistribution of resources in 2002 in the immediate aftermath of 9/11. For 2002, the district response rate for providing data was only 54% compared to 69% for 2003 and the PEP provision rate was only 59% in 2002 compared to 89% in 2003.

The type and completeness of data provided varied among districts. The majority of districts provided paper records of PEP patient data (75%) that required manual review and interpretation, a potential source of information bias. Information recorded in PEP patient records may have been subject to interviewer and recorder bias resulting from the methods of solicitation and interpretation by healthcare providers and recall bias from PEP patients' memory and account of exposure circumstances. Only 25% of the districts sent Excel spreadsheets of aggregate data; most of those were missing data on many variables. Because many districts do not link human rabies PEP data with source animal exposure data and the locations of these data vary within each district, collecting information on all PEP patient variables was problematic. Communication with several persons and departments within a health district was often necessary to obtain both PEP patient data (EPI-1 forms and patient health records) and source animal exposure reports. For example, animal exposure reports may be collected and stored at environmental health offices in some local health departments (LHDs) and health districts or at police departments or animal control offices in others. In addition, at many health districts and LHDs, there was no standardization for collection of human rabies PEP exposure variables, no method in place to link patient rabies PEP and source animal exposure reports, and no centralized database to aggregate human rabies PEP data. Districts that used the environmental health software provided more complete data, individual computer records, on source animals with details on victims and exposures which made linking data easier, although data was not aggregated. Standardization and centralization of data collection methods would facilitate more efficient and effective surveillance for human rabies PEP.

Analysis of appropriateness of PEP and description of many variables were limited by missing information from PEP patient files. Due to the amount of missing information from

patient PEP records and the variability on types of missing information, we chose to include missing information in the analysis and report total percentages to most accurately represent the data collected. Variables that had 50% or more missing information in PEP records included ethnicity, occupation, whether PEP was completed, circumstance of exposure, activity leading to exposure and anatomical site of exposure. Rabies vaccination status and behavior of source animals was missing from over 70% of PEP records. We were unable to include information on prior PEP patient rabies vaccines or adverse reactions to PEP because this information was missing from more than 90% of records.

The number of PEP records provided to the study compared to PEP reported to DZEE [74% (838/1139)], was better than we expected. This may be attributed to the active methods employed for data gathering in this study, by e-mail and telephone communications. Although data extraction was not blinded, we created and adhered to a detailed data collection instrument throughout data extraction to help maintain objectivity and consistency.

The large number of human rabies PEP treatments reported in Virginia in 2002 and 2003 and large numbers of source animals that are not captured suggest that new strategies for education of the public, health care providers and public health staff may help reduce these numbers. Human rabies PEP treatments are time-consuming, labor intensive, unpleasant for patients and carry risk for adverse reactions. PEP treatments are expensive and HRIG and rabies vaccines are often in short supply. Based on 1998 estimates for PEP treatment (emergency room, physician fees and biologics), we estimate the total direct costs to patients and insurers in Virginia for 110 cases of inappropriate PEP in 2003 was between $114,000 and $489,000.[10] This is an underestimate of costs because the 2003 district response rate was 69%, PEP provision rate was 89%, 22.3% of 2003 PEP could not be analyzed due to missing data and these figures are based

on 1998 total treatment costs. Overall, 498 PEP resulting from source animals not captured or with unknown capture status in our study cost patients and insurers in Virginia an estimated $516,000 to $2.2 million for PEP treatments in 2002 and 2003 combined. Rabies infection in humans is 100% fatal but is uncommon in the United States and most rabies cases result from unrecognized exposures. No documented human rabies cases have resulted from indirect, secondary or non bite exposures.[39] Appropriate PEP treatment decisions rely primarily on assessing the risks of a true exposure to a rabid or potentially rabid animal, but also on weighing the benefits and costs of treatment if the patient was not truly exposed.

One approach to reducing the number of PEP resulting from not true exposures and animals that are not captured would be the development by health districts of multiple strategies for ongoing continuing education of health care professionals, ED personnel, and public health staff on the evaluation of animal exposures, the reporting of animal exposures, follow-up on source animals and appropriate administration of PEP. Ready access to the 1999 ACIP recommendations and *2004 VDH Rabies Control Guidelines* definitions of true exposures is recommended. Districts may want to recommend that EDs post ACIP guidelines, the current *VDH Rabies Control Guidelines*, and 24 hour contact telephone numbers for LHDs in obvious and easily accessible locations. Health care providers should be encouraged to report all exposures to potentially rabid animals to the LHD and consult with public health staff in the evaluation of difficult PEP decisions. The high turnover of personnel in EDs calls for frequent continuing education on rabies prevention and PEP decisions. Targeting the health care providers and LHDs in rural areas of Virginia for continuing education, training and support on appropriate assessment of rabies exposures is of particular importance.

The circumstances and activities of human behavior (approaching and touching animals and secondary exposures) that led to a great deal of the PEP in this study indicate that much PEP can be prevented through public health education. We recommend that public health education on rabies prevention continue to emphasize that people not approach, handle or feed any wild animals and any unfamiliar, stray or feral domestics, but rather report the animals to animal control or authorities. Education about not touching objects or animals that may be contaminated with body fluids from a potentially rabid animal and not separating fighting animals is also important. Programs and campaigns that target all human populations but particularly those with potential outdoor exposures are recommended and possible venues include school health and physical education classes, community centers where outdoor sports activities are held, garden clubs, hiking clubs, parks and other outdoor related localities and activities.

In addition to meeting the purpose and objectives of this study, we have described several areas related to human rabies postexposure prophylaxis surveillance and treatment decisions in Virginia requiring further research and consideration. Improvements in the standardization and centralization of data collection methods for human rabies PEP in Virginia is recommended to facilitate future surveillance activities. The many communications with Virginia health district directors and public health personnel involved in human rabies PEP have resulted in increased awareness and attentiveness to PEP decisions, record keeping and data collection methods throughout many districts in Virginia. As a result of this study, the Director of the Division of Zoonotic and Environmental Epidemiology (DZEE) of the Virginia Department of Health assembled a work group to address human rabies PEP surveillance. The responsibility of this new work group is to develop standard and practical approaches to handling rabies PEP data and

follow-up in Virginia. It is the hope of the author that the areas of concern revealed in this study will be addressed by the PEP work group.

TABLES

TABLE 1. Virginia Health Districts that Provided Data and PEP Records Provided by Region, 2002 and 2003

		2002			2003		
Region	Total # VA Health Districts N	# VA Districts Providing Data to Study N (%)	# PEP Reported to DZEE N	# PEP Records Provided to Study N (%)	# VA Districts Providing Data to Study N (%)	# PEP Reported to DZEE N	# PEP Records Provided to Study N (%)
Northwest	5	4 (80)	129	75 (58)	4 (80)	167	122 (73)
Northern	5	3 (60)	83	58 (70)	4 (80)	89	93 (104)
Southwest	9	5 (56)	128	82 (64)	7 (78)	151	118 (78)
Central	7	4 (57)	84	59 (70)	4 (57)	57	44 (77)
Eastern	9	3 (33)	162	70 (43)	5 (56)	89	117 (131)
Total	35	19 (54)	586	344 (59)	24 (69)	553	494 (89)

Note. PEP = Human Rabies Postexposure Prophylaxis, DZEE = Division of Zoonotic and Environmental Epidemiology
* The 2002 and 2003 sample: n = 838 PEP provided, a response rate of 73.6% of 1139 PEP records reported to DZEE.

TABLE 2. Estimated Annual Crude and Age-specific Incidence Rates of PEP by Region, 2003*

Regions [# districts that provided/# in region (%)]	2003 PEP Records Provided to Study N	Population† N	2003 Estimated Annual Rate of PEP Rate/100,000
Total PEP			
Northwest [4/5 (80%)]	122	810316	15.1
Northern [4/5 (80%)]	93	1555177	6.0
Southwest [7/9 (77.8%)]	118	951561	12.4
Central [4/7 (57%)]	44	829416	5.3
Eastern [5/9 (55%)]	117	1166407	10.0
Total	494	5312877	9.3
Child PEP (<18 years)‡			
Northwest [4/5 (80%)]	43	202071	21.3
Northern [4/5 (80%)]	22	376182	5.8
Southwest [7/9 (77.8%)]	36	211185	17.0
Central [4/7 (57%)]	11	208114	5.3
Eastern [5/9 (55%)]	22	304672	7.2
Total	134	1302224	10.3
Adult PEP (>17 years)‡			
Northwest [4/5 (80%)]	76	608245	12.5
Northern [4/5 (80%)]	57	1178995	4.8
Southwest [7/9 (77.8%)]	73	740376	9.9
Central [4/7 (57%)]	28	621302	4.5
Eastern [5/9 (55%)]	77	861735	8.9
Total	311	4010653	7.8

* 2003 sample: N = 494 PEP from 24 districts that provided PEP.
† Source. Population figures represent those 24 districts providing data to the study and are based on Total Virginia Population 2002, Virginia Department of Health, Health Statistics/Statistical Reports and Tables (38).
‡ The 2003 sample had 9.9% (49/494) PEP missing information on age.

TABLE 3. Demographic Characteristics of the 2002 and 2003 PEP Samples

Demographic Variables	Total PEP (N = 838)	%	2002 PEP (N = 344)	%	2003 PEP (N = 494)	%
Region of Virginia						
Northwest	197	23.5	75	21.8	122	24.7
Northern	151	18.0	58	16.9	93	18.8
Southwest	200	23.9	82	23.8	118	23.9
Central	103	12.3	59	17.2	44	8.9
Eastern	187	22.3	70	20.3	117	23.7
Age (years)						
Mean (SD)	32.3 (20.6)		31.2 (19.7)		33 (21.2)	
Median (Range)	31.0 (0.2, 97.0)		30.0 (0.2, 85.0)		32.0 (1.0. 97.0)	
Infant (<1)	3	0.4	2	0.6	1	0.2
Child (1-17)	207	24.7	74	21.5	133	26.9
Adult (>18)	530	63.2	219	63.7	311	63.0
Missing*	98	11.7	49	14.2	49	9.9
Gender of Patient						
Female	412	49.2	163	47.4	249	50.4
Male	377	45.0	159	46.2	218	44.1
Missing*	49	5.8	22	6.4	27	5.5

Note. SD = standard deviation

* Missing information is included for variables with more than 5% missing data.

TABLE 4. Exposure Characteristics of the 2002 and 2003 PEP Samples

Exposure Variables	Total PEP (N = 838)	%	2002 PEP (N = 344)	%	2003 PEP (N = 494)	%
Type of Exposure						
True Exposure	559	66.7	227	66.0	332	67.2
Not True Exposure	149	17.8	62	18.0	87	17.6
Missing*	130	15.5	55	16.0	75	15.2
Type of Exposure Categories						
True Exposure						
Bite	478	57.0	196	57.0	282	57.1
Saliva or body fluid on mucous membrane or in open wound	35	4.2	13	3.8	22	4.4
Suspect Bat	46	5.5	18	5.2	28	5.7
Subtotal	559	66.7	227	66.0	332	67.2
Not True Exposure						
Saliva	19	2.3	10	2.9	9	1.8
Scratch	36	4.3	17	4.9	19	3.8
Touching animal	47	5.6	20	5.8	27	5.5
Body fluid	8	1.0	3	0.9	5	1.0
Secondary exposure	39	4.7	12	3.5	27	5.5
Subtotal	149	17.8	62	18.0	87	17.6
Missing*	130	15.5	55	16.0	75	15.2
Number in Exposure Group						
1 person	533	63.6	239	69.5	294	59.5
>1 person	257	30.7	94	27.3	163	33.0
Missing*	48	5.7	11	3.2	37	7.5

* Missing information is included for variables with more than 5% missing data.

TABLE 5. Source Animal Characteristics, 2002 and 2003*

	Source Animals	
	N	**%**
Domestic or Wild Source Animal (N = 593)†		
Domestic	412	72.2
Wild	159	27.8
Captured for Observation and/or Testing (N = 593)		
Yes	175	29.5
No	337	56.8
Missing	81	13.7
Rabies Positive Among those Captured (N = 175)†		
Yes	130	76.5
No	40	23.5
Primary Behavior Exhibited among Rabies Positive Source Animals (N = 130)		
Aggressive	38	29.2
Sick	15	11.5
Other‡	7	5.4
Missing	70	53.8

* In the 2002 and 2003 sample, 593 animals were associated with 788 PEP. Excludes 1 human.
† Less than 5% missing information in category.
‡ *Other* is a collapsed category for injured, neurological signs, dead, and overly friendly.

TABLE 6. Rabies Status by Species of Animal and PEP Administered, 2002 and 2003

	Rabies Positive					Rabies Negative				
	Animals Tested		PEP Administered			Animals Tested		PEP Administered		
Captured Species	N	%	N	%	Ratio PEP:Animal	N	%	N	%	Ratio PEP:Animal
Domestic†										
Cat	44	34.1	106	37.6	2.4	13	34.2	16	34.0	1.2
Dog	12	9.3	45	16.0	3.8	18	47.4	18	38.3	1.0
Other	2	1.6	9	3.2	4.5	1	2.6	4	8.5	4.0
Subtotal	58	45.0	160	56.7	2.8	32	84.2	38	80.9	1.2
Wild										
Raccoon	37	28.7	67	23.8	1.8	0	0.0	0	0.0	0.0
Bat	11	8.5	21	7.4	1.9	5	13.2	8	17.0	1.6
Fox	11	8.5	16	5.7	1.5	0	0.0	0	0.0	0.0
Skunk	7	5.4	9	3.2	1.3	0	0.0	0	0.0	0.0
Other	5	3.9	9	3.2	1.8	1	2.6	1	2.1	1.0
Subtotal	71	54.9	122	43.3	1.7	6	15.8	9	19.1	1.5
Total*†	129	100.0	282	100	2.2	38	100.0	47	100	1.2

*Information was missing for 8 captured animals

† Domestic does not include 1 human with rabies

TABLE 7. Inappropriate and Appropriate PEP by Patient Demographic and Exposure Characteristics, 2003*†

	Inappropriate PEP (N = 110)	%	Appropriate PEP (N = 270)	%	Total PEP (N = 380)	%	Chi Square	p-value‡
Demographic Variables								
Region of Virginia							15.87	0.003
Northwest	32	29.1	53	19.6	85	22.4		
Northern	9	8.2	46	17.0	55	14.5		
Southwest	39	35.5	62	23.0	101	26.6		
Central	7	6.4	31	11.5	38	10.0		
Eastern	23	20.9	78	28.9	101	26.6		
Exposure Variables								
Type of Exposure							276.95	<0.001
True	23	20.9	270	100.0	293	77.1		
Not True	87	79.1	-	-	87	22.9		
Number in Exposure Group§							32.87	<0.001
1 person	45	41.3	196	72.6	241	63.4		
>1 person	64	58.7	74	27.4	138	36.3		

* Excluded 2 PEP resulting from human exposures and 3 PEP from wolf hybrid exposures.

† 2003 Sample analyzed for appropriateness of PEP 380/489 = 77.7% : Appropriate PEP = 270/489 = 55.2%, Innappropriate PEP 110/489 = 22.5%, Missing information 109/489 = 22.3%.

‡ p - values calculated from Pearson chi square test of proportions, analyzed at $\alpha = 0.05$ significance level.

§ Less than 5% missing in category.

TABLE 8. Comparison of Source Animals in Inappropriate and Appropriate PEP Groups by Source Animal Characteristics, 2003*†

	Source Animals						
	Inappropriate PEP		Appropriate PEP		Total	Chi	p-value§
Source Animal Characteristics	(N = 59)	%	(N = 216)	%	(N = 275)	Square	
Domestic or Wild Source Animal						10.1	0.001
Domestic	33	55.9	166	76.9	199		
Wild	26	44.1	50	23.1	76		
Captured for Observation and/or Test‡						90.9	<0.001
Yes	48	84.2	39	18.1	87		
No	9	15.8	177	81.9	186		
Ownership status						28.7	<0.001
Owned	18	32.1	24	11.1	42		
Stray or Feral	12	21.4	117	54.2	129		
Wild	26	46.4	50	23.1	76		
Missing	3	5.0	25	11.6	28		
Rabies Positive (of those captured)						25.3	<0.001
Yes	26	53.1	40	100.0	66		
No	23	46.9	-	-	23		
Missing	10	16.9	176	81.0	186		

* Does not include 1 human and 1 wolf hybrid.

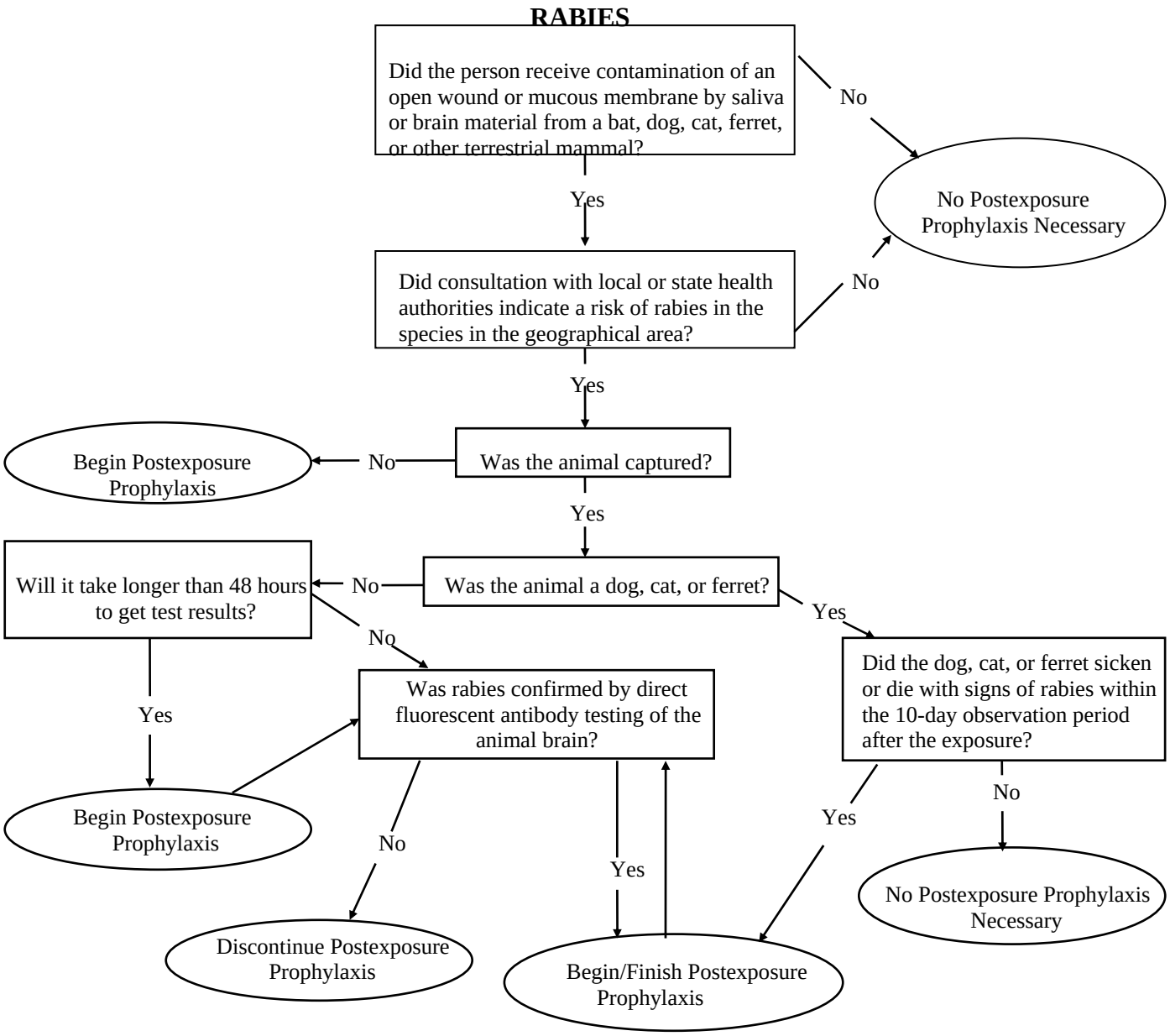
† 275 animals represented 379 PEP analyzed for appropriateness of PEP.

‡ Less than 5% missing information in category.

§ p - values calculated from chi square test of proportions, analyzed at $\alpha = 0.05$ significance level.

FIGURES

FIGURE 1. Algorithm: Human Rabies Postexposure Treatment



Source: 2004 Virginia Rabies Control Guidelines, Virginia Department of Health **(15)**

FIGURE 2a. Health Districts that Provided PEP Data, 2003

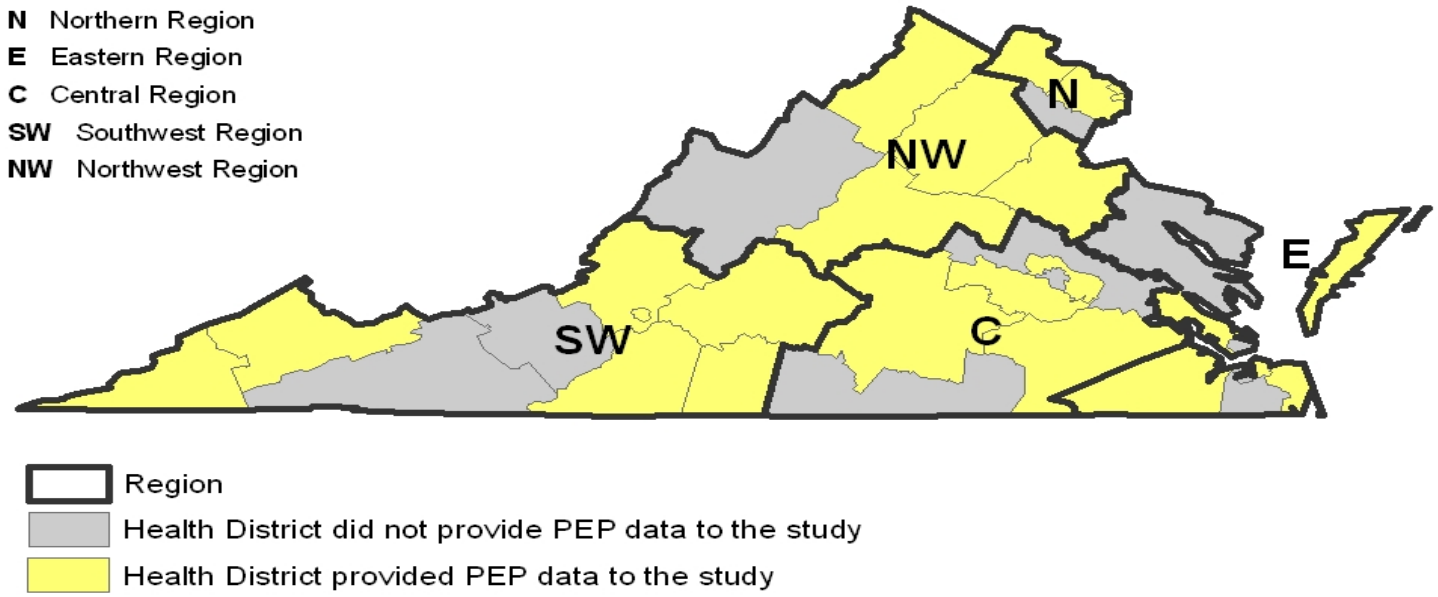
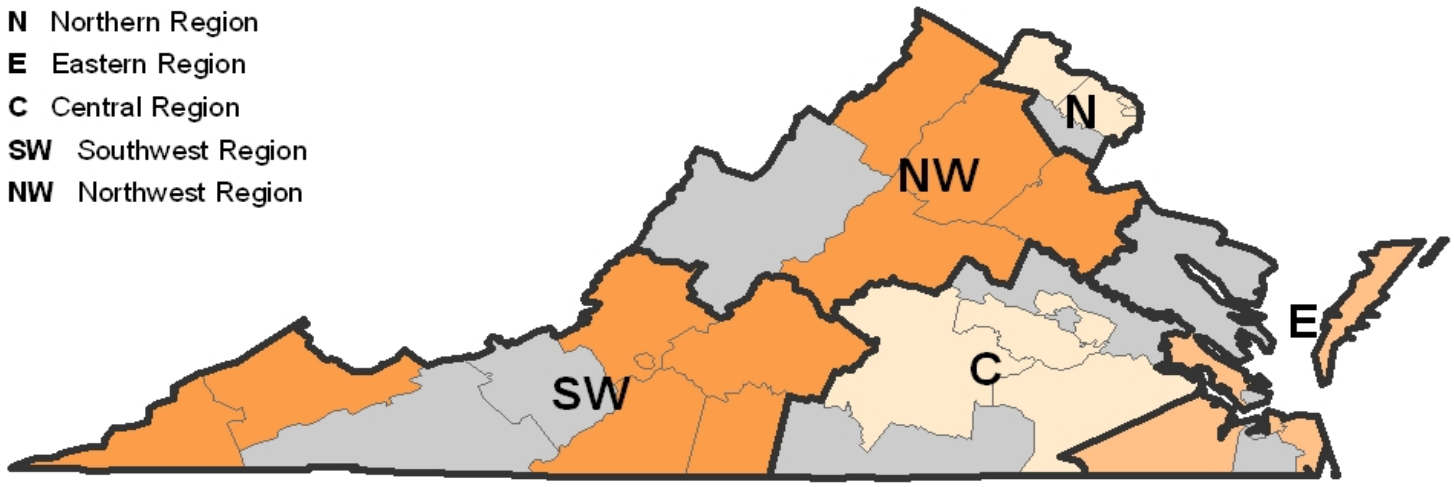
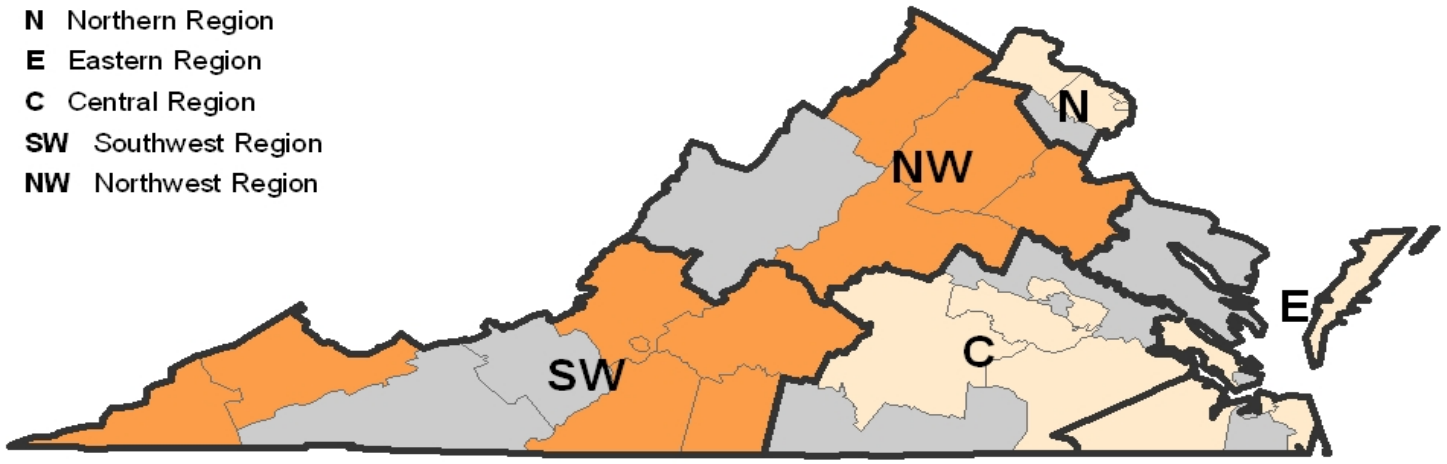


FIGURE 2b. Crude Incidence Rates of PEP by Region, 2003*



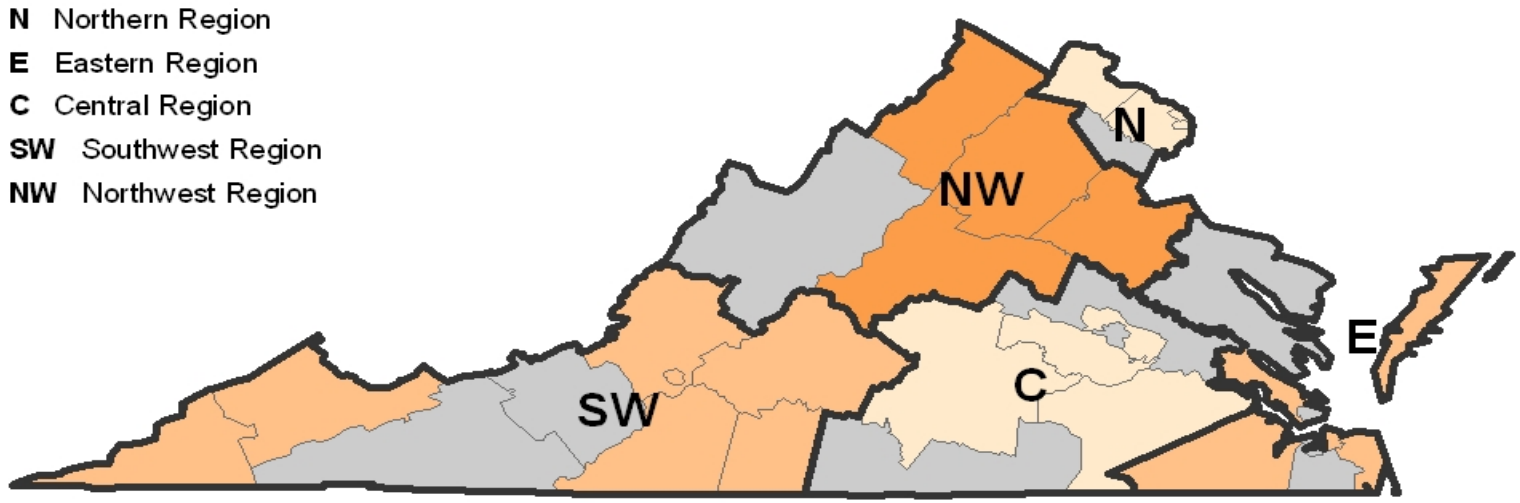
**Rates represent only those districts that provided data within each region.*
Source: Total Virginia population 2002, Virginia Department of Health, Health Statistics/ Statistical Reports and tables^35

FIGURE 2c. PEP Incidence Rates for Children by Region, 2003*



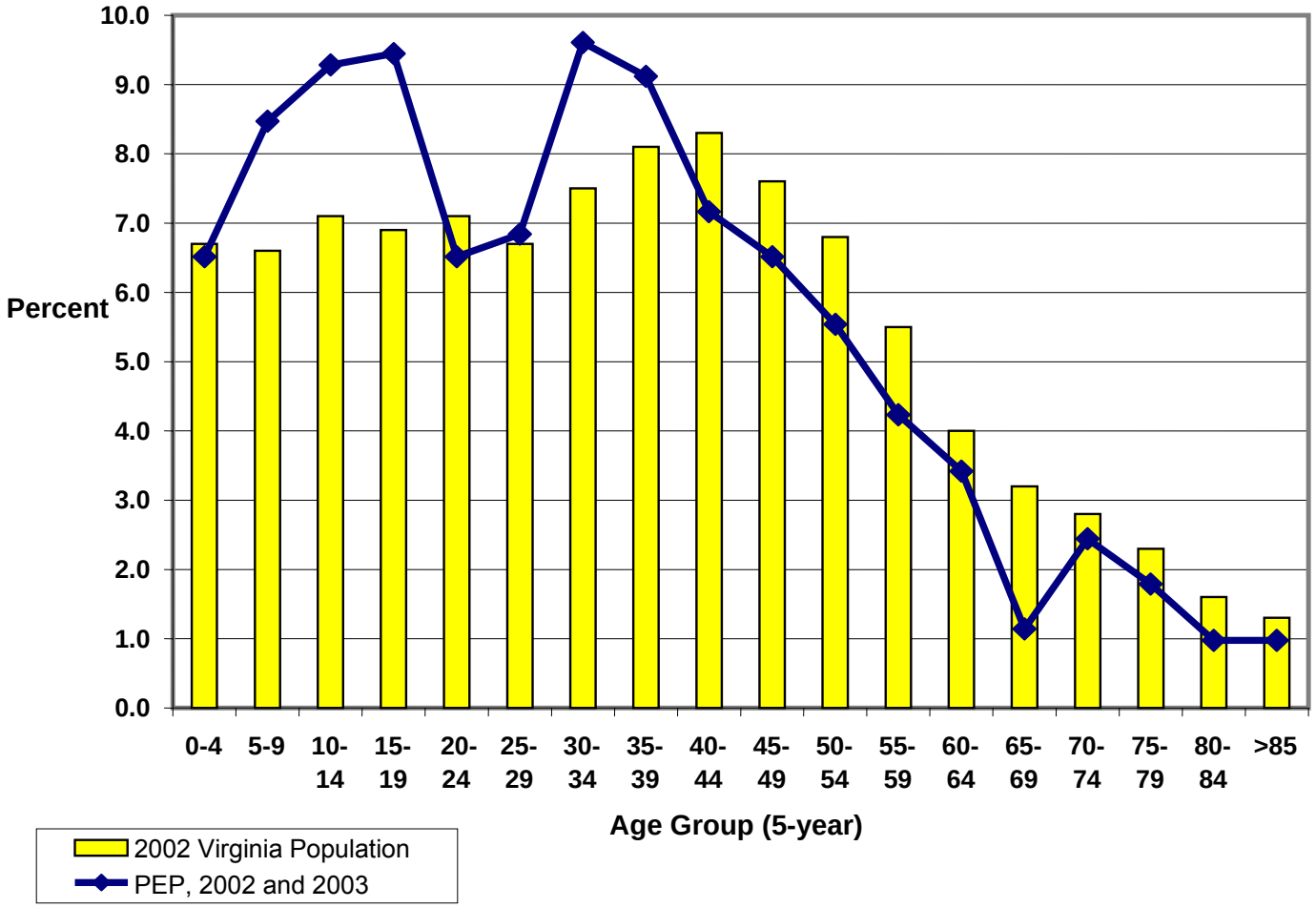
**Rates represent only those districts that provided data within each region.*
Source: Total Virginia population 2002, Virginia Department of Health, Health Statistics/ Statistical Reports and tables^35

FIGURE 2d. PEP Incidence Rates for Adults by Region, 2003*



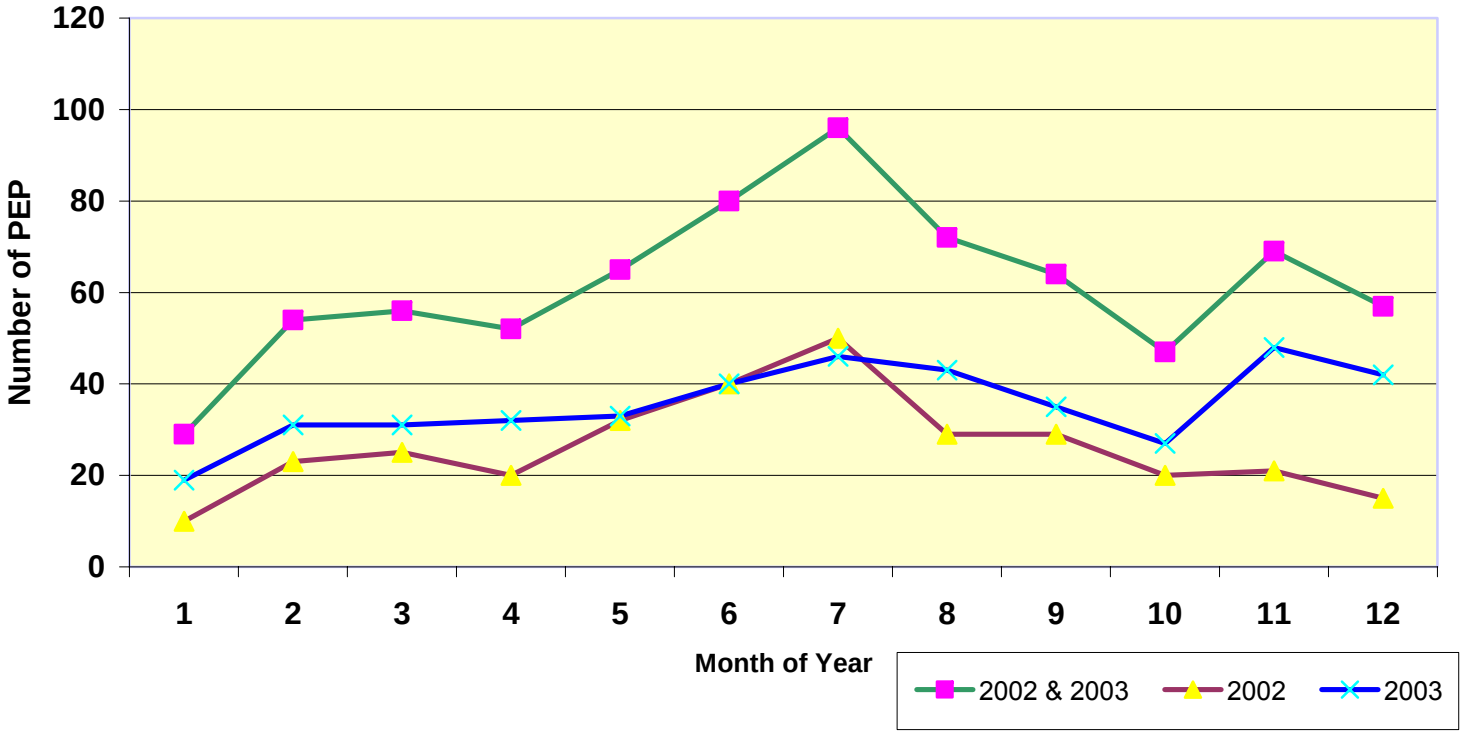
*Rates represent only those districts that provided data within each region.
Source: Total Virginia population 2002, Virginia Department of Health, Health Statistics/ Statistical Reports and tables^35

FIGURE 3. Percent PEP and 2002 Virginia Population by 5-year Age Groups, 2002 and 2003*



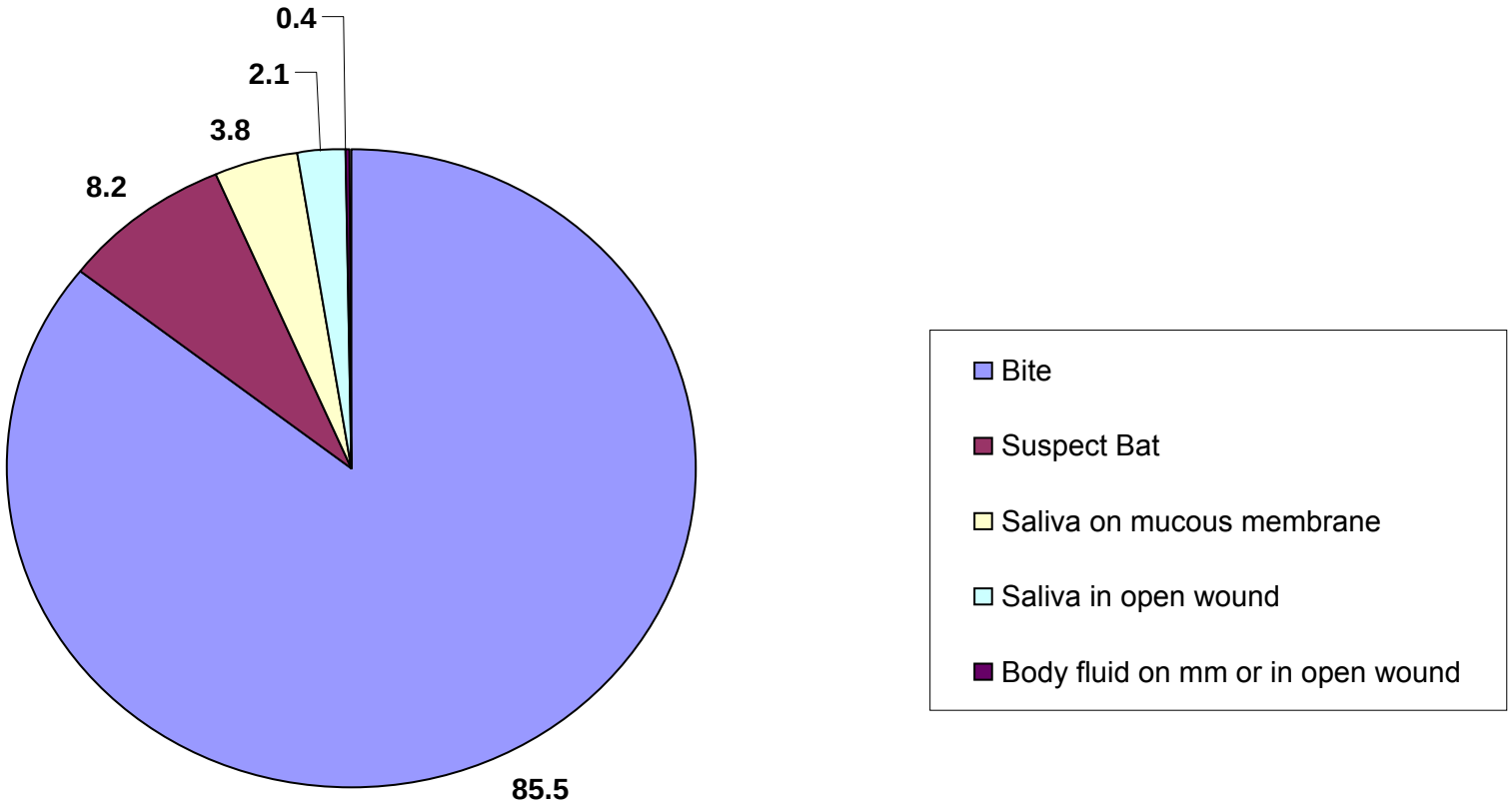
*5-year age information available for N = 614 PEP (26.6%, 224/838 PEP missing data)
Source: VDH. Total Virginia Population 2002, Health Statistics/Statistical Reports and Tables (38)

FIGURE 4. PEP by Month of Exposure, 2002 and 2003*



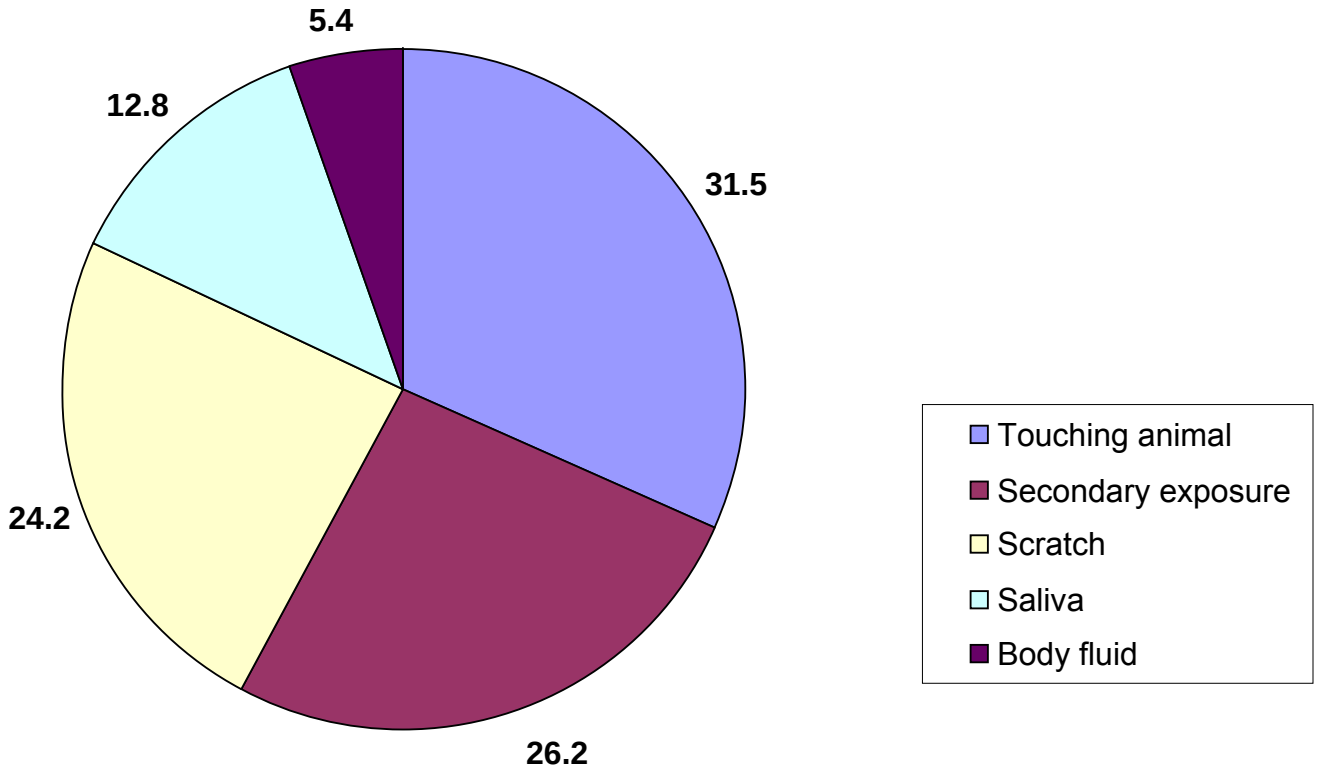
* Month of exposure available for N = 741 PEP (11.6% (97/838) PEP missing data)

FIGURE 5a. True Exposures
Percent PEP by Type of Exposure
2002 and 2003*



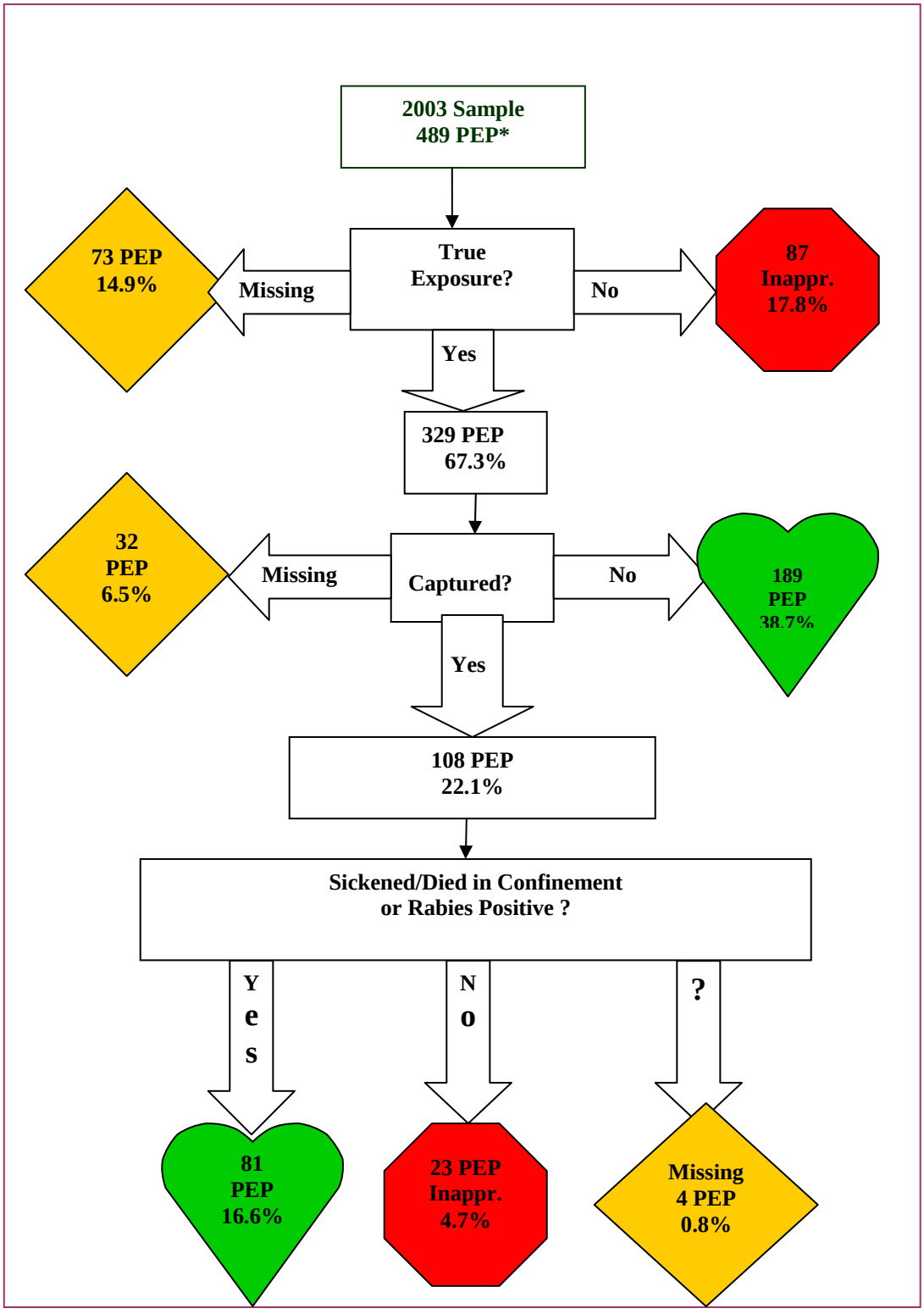
*True Exposures: N = 559 PEP
Body fluid – Indicated when an exposure to saliva and/or CNS material could not be ruled out.

FIGURE 5b. Not True Exposures
Percent PEP by Type of Exposure
2002 and 2003*



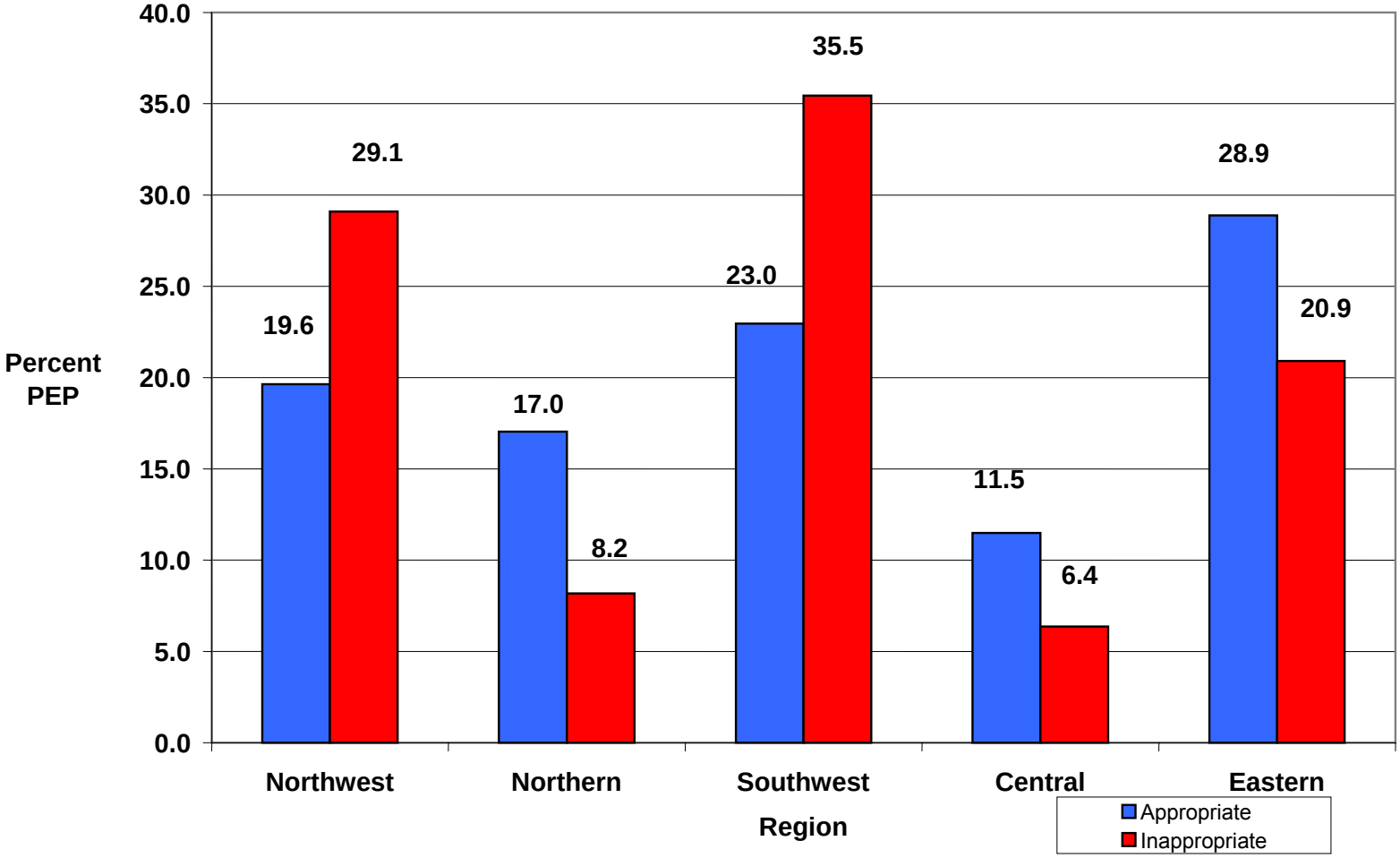
* Not True Exposures: N = 149

FIGURE 6. Flowchart for 2003 Appropriateness of PEP Algorithm



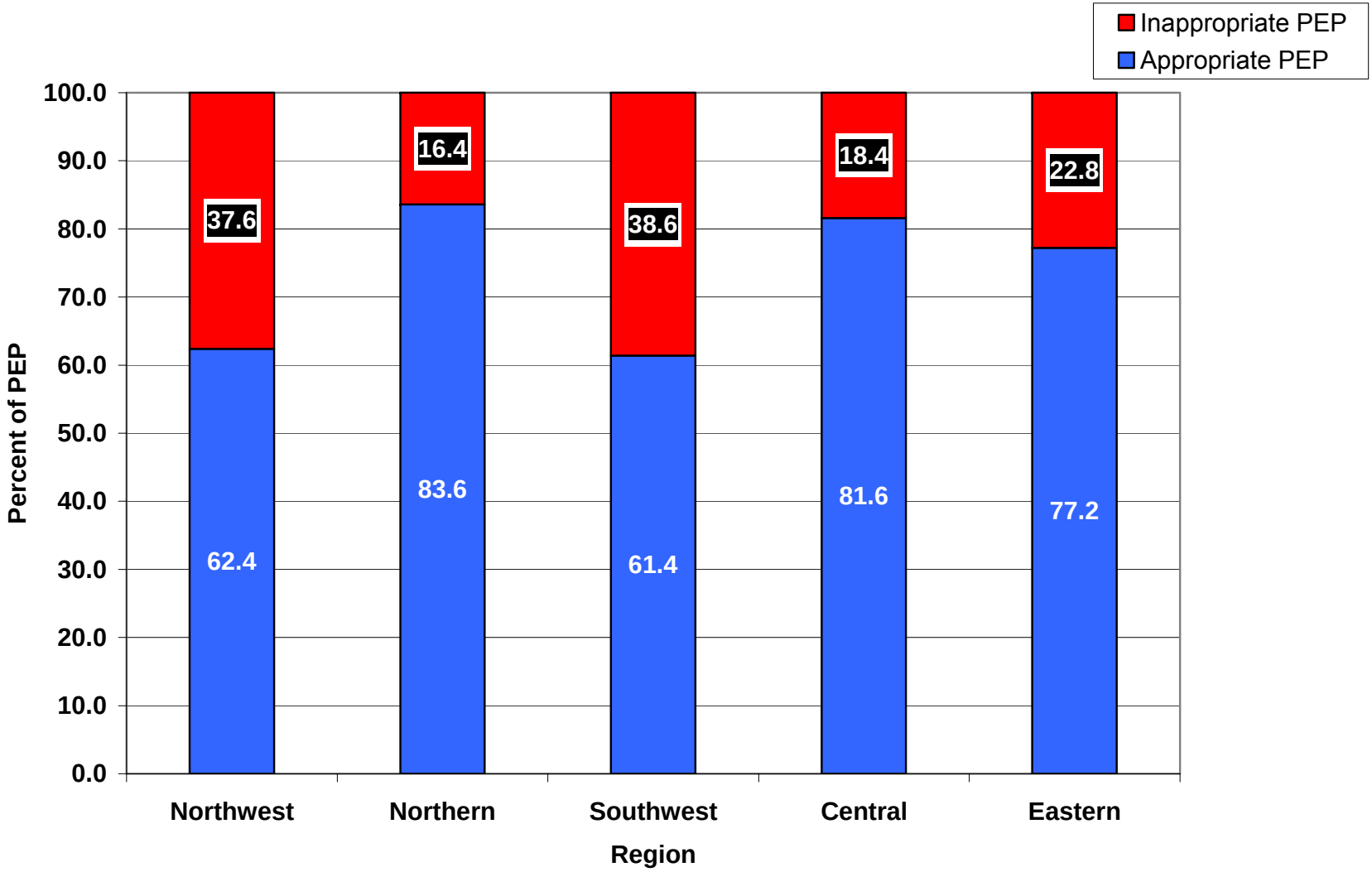
* Excludes 2 PEP from human exposures, and 3 PEP from wolf hybrid exposures

FIGURE 7a. Percent Appropriate and Inappropriate PEP among Regions, 2003*



* The 2003 sample: N = 380 PEP analyzed for appropriateness of PEP

FIGURE 7b. Percent Appropriate and Inappropriate PEP by Region, 2003*



* The 2003 sample: N = 380 PEP analyzed for appropriateness of PEP

APPENDIX A

Appendix A. Data Collection Instrument
The Epidemiology of Human Rabies Postexposure Prophylaxis (PEP)
in Virginia, 2002 and 2003

I. Rabies Postexposure Prophylaxis (PEP)

1. Date PEP initiated:_____Month , Day, Year (00-00-00)

2. Rabies Vaccination Status
    1. Never vaccinated (Never)
    2. Pre-exposure vaccinated (Pre-exp)
    3. Previous PEP (PrevPEP)
    4. Unknown

3. PEP completed?
    1. Yes
    2. No
    3. Unknown

4. Local Adverse Reactions (injection site reactions)?
    1. Pain
    2. Erythema
    3. Swelling
    4. Itching
    5. Bruise
    6. Unknown = not reported

5. General Systemic Adverse Reactions?
    1. Headache
    2. Nausea
    3. Abdominal pain
    4. Vomiting
    5. Muscle aches
    6. Dizziness
    7. Sweat
    8. Anxious
    9. Dyspnea
    10. Unknown = not reported

6. Central Nervous System Reactions_____
_____

7. Peripheral Nervous System Reactions _____
_____

8. Immune Complex-like Reactions
    1. Generalized urticaria
    2. Arthralgia
    3. Arthritis
    4. Angioedema
    5. Nausea
    6. Vomiting
    7. Fever
    8. Malaise
    9. Other_____
    10. Unknown

II. Human PEP Patient Demographic Data

1. County/city of residence:_____

2. Age___ (if numerical age not given then indicate adult or child)

3. Gender
    1. Female
    2. Male
    3. Unknown

4. Race
    1. White (Caucasian)
    2. Black (African-American)
    3. American Indian or Alaskan Native
    4. Native Hawaiian or Pacific Islander
    5. Asian
    6. Other
    7. Unknown

5. Ethnicity
    1. Hispanic (Hispanic)
    2. Non-Hispanic (Non)

6. Occupation:
    1. None
    2. NA – child
    3. Unemployed
    4. Retired
    5. Disabled
    6. Veterinarian
    7. Vet. Staff (Vet. Assistant, or Vet. Tech)
    8. Wildlife Rehabilitator
    9. Animal Control/Caretaker
    10. Other

III. Rabies Exposure Factors and Circumstances of Exposure for person receiving PEP

1. Date of exposure: _____Month, Day, Year (00/ 00/ 00)

2. County/City of exposure: _____

3. Anatomical site of exposure: (Circle all that apply)
    1. Head/neck (to include face)
    2. Arm/hand (to include wrist, shoulder)
    3. Leg/foot (to include ankle)
    4. Torso
    5. Potential Bat Contact (PotBat) no anatomical site recognized
    6. Unknown (anatomical site not known)

4. Type of exposure: (Circle all that apply)
    1. Single bite (Bite)
    2. Multiple bites (Multbites)
    3. Scratch with unknown contamination (Scratch)
    4. Scratch with Saliva contamination (Scratch/Sal)
    5. Scratch with central nervous system (CNS) tissue contamination (Scratch/CNS)
    6. Open Wound with Saliva contamination (Wound/Sal)
    7. Open Wound with CNS tissue contamination (Wound/CNS)
    8. Saliva on mucous membrane (Sal/mm) saliva on eye, mouth, nose
    9. CNS tissue on mucous membrane (CNS/mm)
    10. Touching animal (Touchani) = except bats and assuming no saliva on mm or in wound
    11. Skinning/dressing animal (Skinning)
    12. Potential Bat Contact (PotBat) = handled (direct contact) or in room or vehicle with bat
    13. Secondary Exposure (secondexp) = exposed to animal or fomite with saliva contamination
    14. Blood (no mm or wound contact)
    15. Saliva (no mm or wound contact)
    16. Body Fluid (BodyFluid) = Blood, Urine, Feces, Saliva no distinction made (no mm or wound contact)
    17. Unknown

5. Circumstances of exposure:
    1. Person approached animal (persappr)
    2. Animal approached person (animappr)
    3. Potential Bat Contact (PotBat) = Bat in house etc, unrecog. Exp.
    4. Secondary Exposure = saliva on fomites, potential exposure to saliva from source animal on victim’s pet or other animal
    5. Unknown

6. Occupation-related exposure? (Exposure occurred at work and occupation may or may not be directly associated with animals.)
    1. Yes
    2. No
    3. Unknown

7. Person's activity leading to exposure:
    1. Handling (handling) = includes petting, caring for (giving shots)
    2. Playing with animal (playwi)
    3. Picking up animal (pickup)
    4. Feeding animal (feedanim)
    5. Skinning/dissecting animal (skinning)
    6. Eating animal (eatingani)
    7. Attacked by animal (attbyani)
    8. Separating fighting animals (sepfiani)
    9. Kissing animal (kissanim)
    11. Other = contact with source animal's saliva on fomites or on animal exposed to source animal; potential bat exposure (bat in house or vehicle or direct contact)
    12. Unknown

IV. Source Animal Factors

1. Species
    1. Raccoon
    2. Skunk
    3. Fox
    4. Bat
    5. Cat
    6. Dog
    7. woodchuck (groundhog)
    8. beaver
    9. Opossum
    10. Rat
    11. Horse
    12. Bovine – Cattle
    13. Captive wild species_____
    14. Wild hybrid = Wolf Hybrid
    15. Unknown

2. Available for observation and testing?
    1. Yes
    2. No (notavail)
    3. Unknown

3. Date animal collected_____ Month/ Day/ Year, or Not Available (NotAvail)

4. Animal Ownership
    1. Stray (includes feral = born in wild)
    2. Owned (domestic species)
    3. Wild animal in wild (wild)
    4. Captive wild species
    5. Unknown

5. Animal has vaccination against rabies?
    1. Yes current (current)
    2. Yes - not current (expired)
    3. No – no vaccines
    4. Unknown
    5. NA = wildlife

6. Animal behavior/health at time of exposure, collection or confinement
    1. Dead
    2. Normal
    3. Abnormal
    4. Unknown

Circle <u>any one or more</u> that apply about animal behavior at capture:
    1. Sick
    2. Aggressive
    3. Overly friendly (ovfr)
    4. Wobbly gait or other neurological signs (neurol)
    5. Paralyzed
    6. Injured
    7. Other_____

7. Was source animal known to be exposed to a confirmed rabid animal?
    1. Yes
    2. No
    3. Unknown

8. Was source animal known to be exposed to a suspect rabid animal?
    1. Yes
    2. No
    3. Unknown

9. Number of persons exposed to source animal: _____

10. Number of domestic animals exposed to source animal: _____

11. Laboratory test results for rabies virus in source animal:
    1. Positive
    2. Negative
    3. Unsatisfactory specimen (unsat) = indeterminate
    4. Not submitted (notsub) = either unavailable for testing because animal at-large or released from confinement/quarantine in negative status
    5. Unknown = not reported

12. Confinement and Observation (dogs, cats, ferrets and livestock)
    1. Confinement period completed, animal released normal (Conf/Rel)
    2. Abnormal behavior during confinement – Test Positive (Conf/Pos)
    3. Abnormal behavior during confinement – Euthanized (Conf/Euth)
    4. Confined – no follow-up (conf/inc)
    5. Not Available for confinement = animal at-large (notavail)
    6. Not Applicable (NA) – (wild species, collected and tested positive)

13. Followed ACIP Recommendation for rabies postexposure prophylaxis
    1. Yes
    2. No = no documentation of saliva or CNS contamination to open wounds or mucous membranes (eyes, nose, mouth) Ex.: handling, picking up, petting, scratch, blood
    3. Unknown = could be in accordance with ACIP recommendations but unable to determine from information given.

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